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FIG.1A

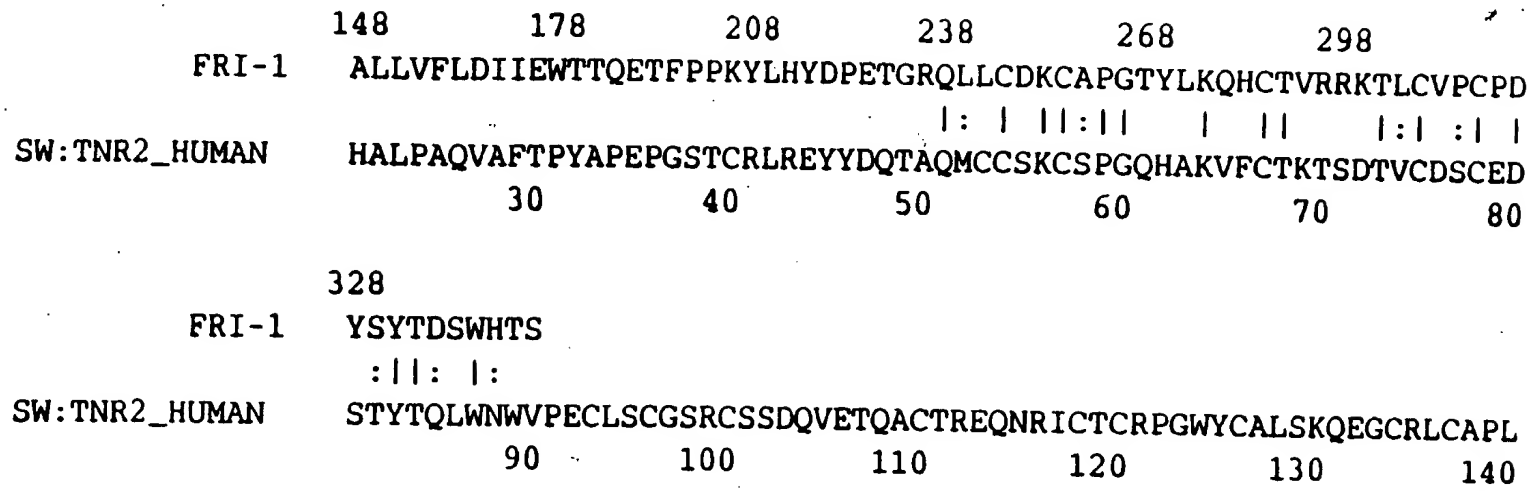


FIG.1B

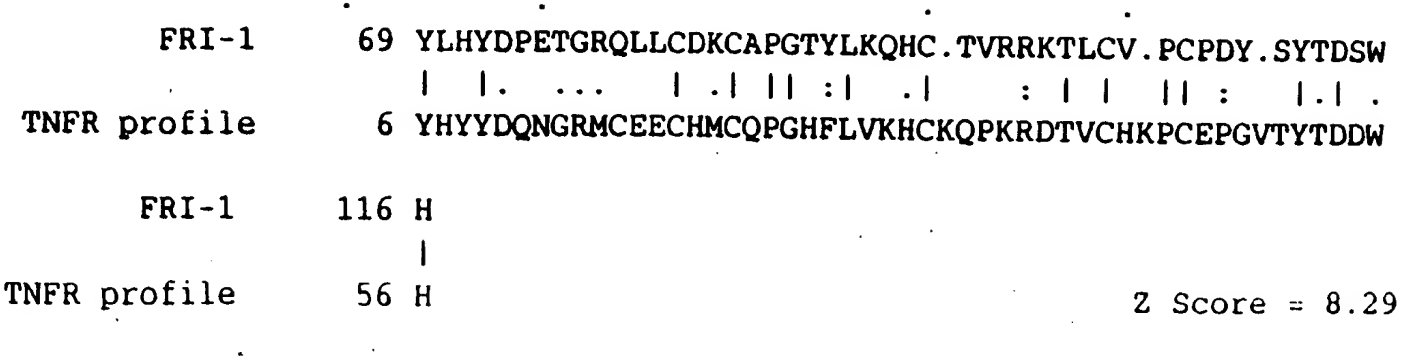


FIG. IC

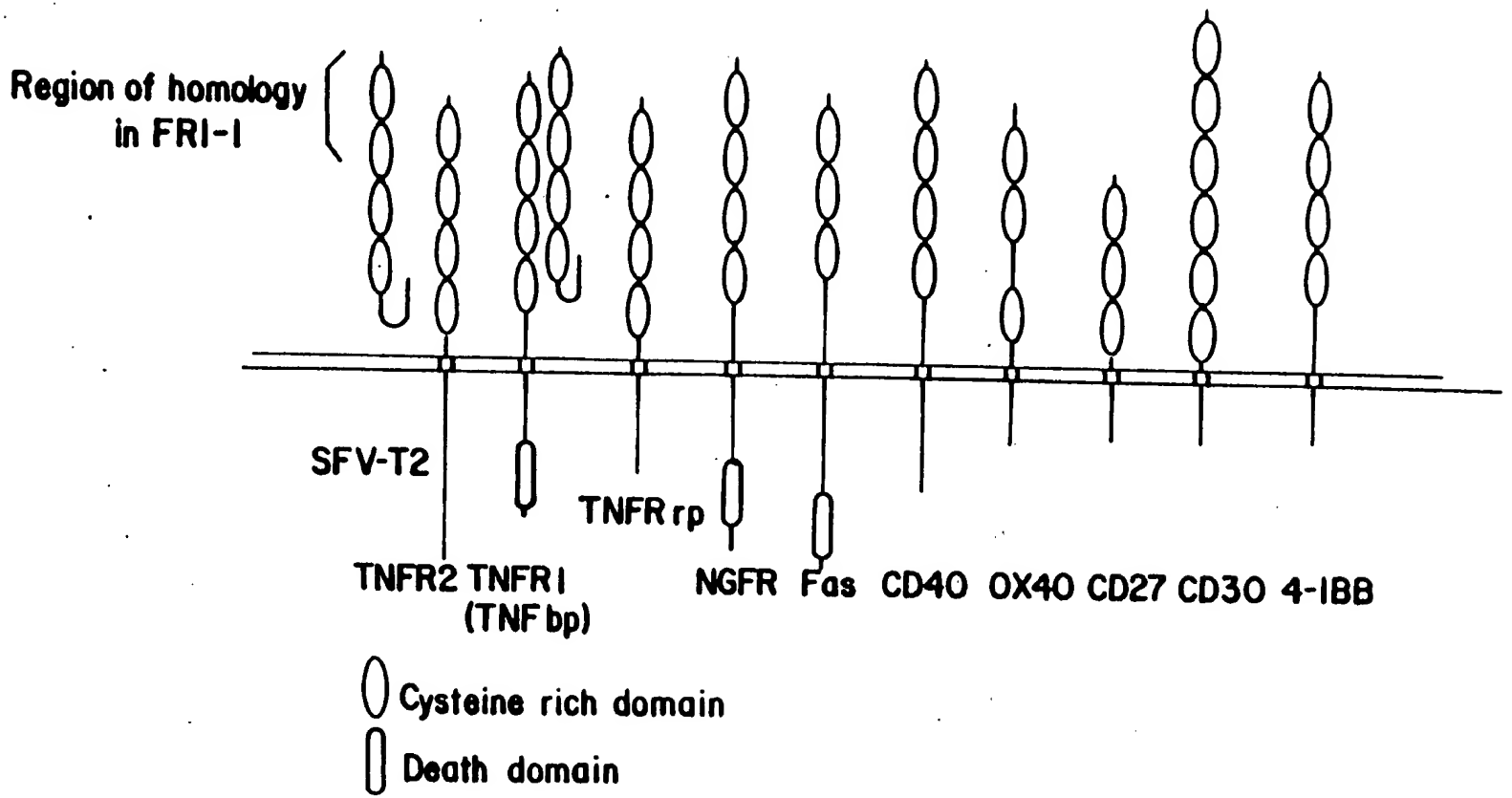


FIG.2A

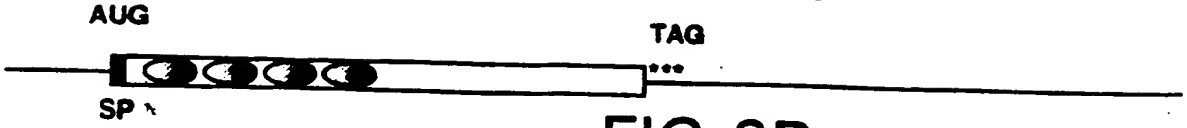


FIG.2B

```
          10                  30                  50
ATCAAAGGCAGGGCATACTTCCTGTTGCCCAGACCTTATATAAAACGTCATGTTCGCCTG
          70                  90                 110
GGCAGCAGAGAAGCACCTAGCACTGGCCCAGCGGCTGCCGCCTGAGGTTTCCAGAGGACC
         130                 150                 170
ACAATGAACAAGTGGCTGTGCTGTGCACTCCTGGTGTTCTTGGACATCATTGAATGGACA
   M  N  K  W  L  C  C  A  L  L  V  F  L  D  I  I  E  W  T
         190                 210                 230
ACCCAGGAAACCTTTCCTCCAAAATACTTGCATTATGACCCAGAAACCGGACGTCAGCTC
T  Q  E  T  F  P  P  K  Y  L  H  Y  D  P  E  T  G  R  Q  L
         250                 270                 290
TTGTGTGACAAATGTGCTCCTGGCACCTACCTAAAACAGCACTGCACAGTCAGGAGGAAG
L  C  D  K  C  A  P  G  T  Y  L  K  Q  H  C  T  V  R  R  K
         310                 330                 350
ACACTGTGTGTCCCTTGCCCTGACTACTCTTATACAGACAGCTGGCACACGAGTGATGAA
T  L  C  V  P  C  P  D  Y  S  Y  T  D  S  W  H  T  S  D  E
         370                 390                 410
TGCGTGTACTGCAGCCCCGTGTGCAAGGAACTGCAGACCGTGAAACAGGAGTGCAACCGC
C  V  Y  C  S  P  V  C  K  E  L  Q  T  V  K  Q  E  C  N  R
         430                 450                 470
ACCCACAACCGAGTGTGCGAATGTGAGGAAGGGCGCTACCTGGAGCTCGAATTCTGCTTG
T  H  N  R  V  C  E  C  E  E  G  R  Y  L  E  L  E  F  C  L
         490                 510                 530
AAGCACCGGAGCTGTCCCCCAGGCTTGGGTGTGCTGCAGGCTGGGACCCCAGAGCGAAAC
K  H  R  S  C  P  P  G  L  G  V  L  Q  A  G  T  P  E  R  N
         550                 570                 590
ACGGTTTGCAAAAGATGTCCGGATGGGTTCTTCTCAGGTGAGACGTCATCGAAAGCACCC
T  V  C  K  R  C  P  D  G  F  F  S  G  E  T  S  S  K  A  P
         610                 630                 650
TGTAGGAAACACACCAACTGCAGCTCACTTGGCCTCCTGCTAATTCAGAAAGGAAATGCA
C  R  K  H  T  N  C  S  S  L  G  L  L  L  I  Q  K  G  N  A
         670                 690                 710
ACACATGACAATGTATGTTCCGGAAACAGAGAAGCAACTCAAAATTGTGGAATAGATGTC
T  H  D  N  V  C  S  G  N  R  E  A  T  Q  N  C  G  I  D  V
         730                 750                 770
ACCCTGTGCGAAGAGGCATTCTTCAGGTTTGCTGTGCCTACCAAGATTATACCGAATTGG
T  L  C  E  E  A  F  F  R  F  A  V  P  T  K  I  I  P  N  W
         790                 810                 830
CTGAGTGTTCTGGTGGACAGTTTGCCTGGGACCAAAGTGAATGCAGAGAGTGTAGAGAGG
L  S  V  L  V  D  S  L  P  G  T  K  V  N  A  E  S  V  E  R
         850                 870                 890
ATAAAACGGAGACACAGCTCGCAAGAGCAAACTTTCCAGCTACTTAAGCTGTGGAAGCAT
I  K  R  R  H  S  S  Q  E  Q  T  F  Q  L  L  K  L  W  K  H
         910                 930                 950
CAAAACAGAGACCAGGAAATGGTGAAGAAGATCATCCAAGACATTGACCTCTGTGAAAGC
Q  N  R  D  Q  E  M  V  K  K  I  I  Q  D  I  D  L  C  E  S
         970                 990                1010
AGTGTGCAACGGCATATCGGCCACGCGAACCTCACCACAGAGCAGCTCCGCATCTTGATG
S  V  Q  R  H  I  G  H  A  N  L  T  T  E  Q  L  R  I  L  M
```

FIG.2C

```
 1030                                     1050                                     1070
GAGAGCTTGCCTGGGAAGAAGATCAGCCCAGACGAGATTGAGAGAACGAGAAAGACCTGC
 E  S  L  P  G  K  K  I  S  P  D  E  I  E  R  T  R  K  T  C
 1090                                     1110                                     1130
AAACCCAGCGAGCAGCTCCTGAAGCTACTGAGCTTGTGGAGGATCAAAAATGGAGACCAA
 K  P  S  E  Q  L  L  K  L  L  S  L  W  R  I  K  N  G  D  Q
 1150                                     1170                                     1190
GACACCTTGAAGGGCCTGATGTACGCACTCAAGCACTTGAAAGCATACCACTTTCCCAAA
 D  T  L  K  G  L  M  Y  A  L  K  H  L  K  A  Y  H  F  P  K
 1210                                     1230                                     1250
ACCGTCACCCACAGTCTGAGGAAGACCATCAGGTTCTTGCACAGCTTCACCATGTACCGA
 T  V  T  H  S  L  R  K  T  I  R  F  L  H  S  F  T  M  Y  R
 1270                                     1290                                     1310
TTGTATCAGAAACTCTTTCTAGAAATGATAGGGAATCAGGTTCAATCAGTGAAGATAAGC
 L  Y  Q  K  L  F  L  E  M  I  G  N  Q  V  Q  S  V  K  I  S
 1330                                     1350                                     1370
TGCTTATAGTTAGGAATGGTCACTGGGCTGTTTCTTCAGGATGGGCCAACACTGATGGAG
 C  L
 1390                                     1410                                     1430
CAGATGGCTGCTTCTCCGGCTCTTGAAATGGCAGTTGATTCCTTTCTCATCAGTTGGTGG
 1450                                     1470                                     1490
GAATGAAGATCCTCCAGCCCAACACACACACTGGGGAGTCTGAGTCAGGAGAGTGAGGCA
 1510                                     1530                                     1550
GGCTATTTGATAATTGTGCAAAGCTGCCAGGTGTACACCTAGAAAGTCAAGCACCCTGAG
 1570                                     1590                                     1610
AAAGAGGATATTTTTATAACCTCAAACATAGGCCCTTTCCTTCCTCTCCTTATGGATGAG
 1630                                     1650                                     1670
TACTCAGAAGGCTTCTACTATCTTCTGTGTCATCCCTAGATGAAGGCCTCTTTTATTTAT
 1690                                     1710                                     1730
TTTTTTATTCTTTTTTTCGGAGCTGGGGACCGAACCCAGGGCCTTGCGCTTGCGAGGCAA
 1750                                     1770                                     1790
GTGCTCTACCACTGAGCTAAATCTCCAACCCCTGAAGGCCTCTTTCTTTCTGCCTCTGAT
 1810                                     1830                                     1850
AGTCTATGACATTCTTTTTTCTACAATTCGTATCAGGTGCACGAGCCTTATCCCATTTGT
 1870                                     1890                                     1910
AGGTTTCTAGGCAAGTTGACCGTTAGCTATTTTTCCCTCTGAAGATTTGATTCGAGTTGC
 1930                                     1950                                     1970
AGACTTGGCTAGACAAGCAGGGGTAGGTTATGGTAGTTTATTTAACAGACTGCCACCAGG
 1990                                     2010                                     2030
AGTCCAGTGTTTCTTGTTCCTCTGTAGTTGTACCTAAGCTGACTCCAAGTACATTTAGTA
 2050                                     2070                                     2090
TGAAAAATAATCAACAAATTTTATTCCTTCTATCAACATTGGCTAGCTTTGTTTCAGGGC
 2110                                     2130                                     2150
ACTAAAAGAAACTACTATATGGAGAAAGAATTGATATTGCCCCCAACGTTCAACAACCCA
 2170                                     2190                                     2210
ATAGTTTATCCAGCTGTCATGCCTGGTTCAGTGTCTACTGACTATGCGCCCTCTTATTAC
 2230                                     2250                                     2270
TGCATGCAGTAATTCAACTGGAAATAGTAATAATAATAATAGAAATAAAATCTAGACTCC
 2290                                     2310                                     2330
ATTGGATCTCTCTGAATATGGGAATATCTAACTTAAGAAGCTTTGAGATTTCAGTTGTGT
 2350                                     2370                                     2390
TAAAGGCTTTTATTAAAAAGCTGATGCTCTTCTGTAAAAGTTACTAATATATCTGTAAGA
 2410                                     2430
CTATTACAGTATTGCTATTTATATCCATCCAG
```

FIG.2D

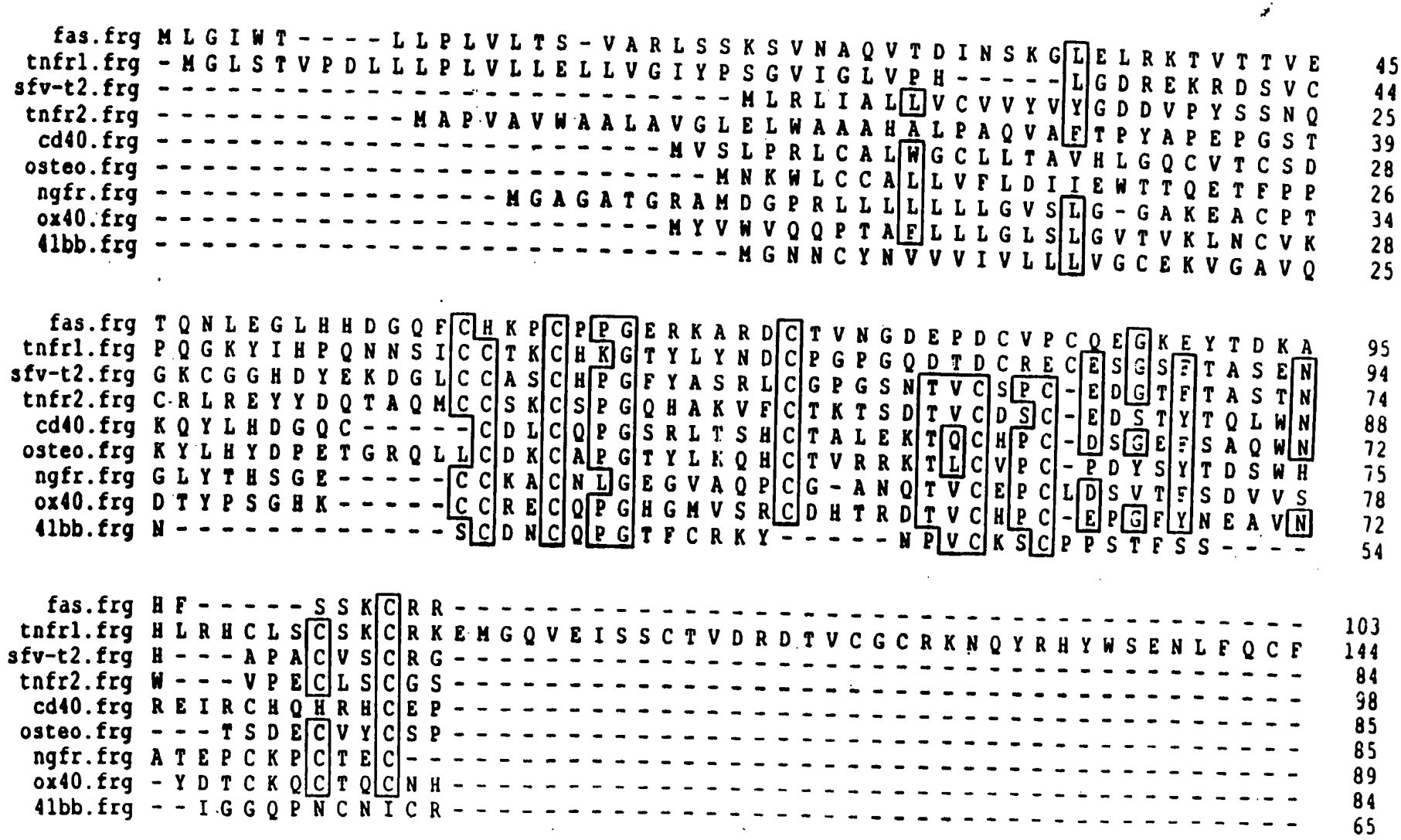


FIG.2E

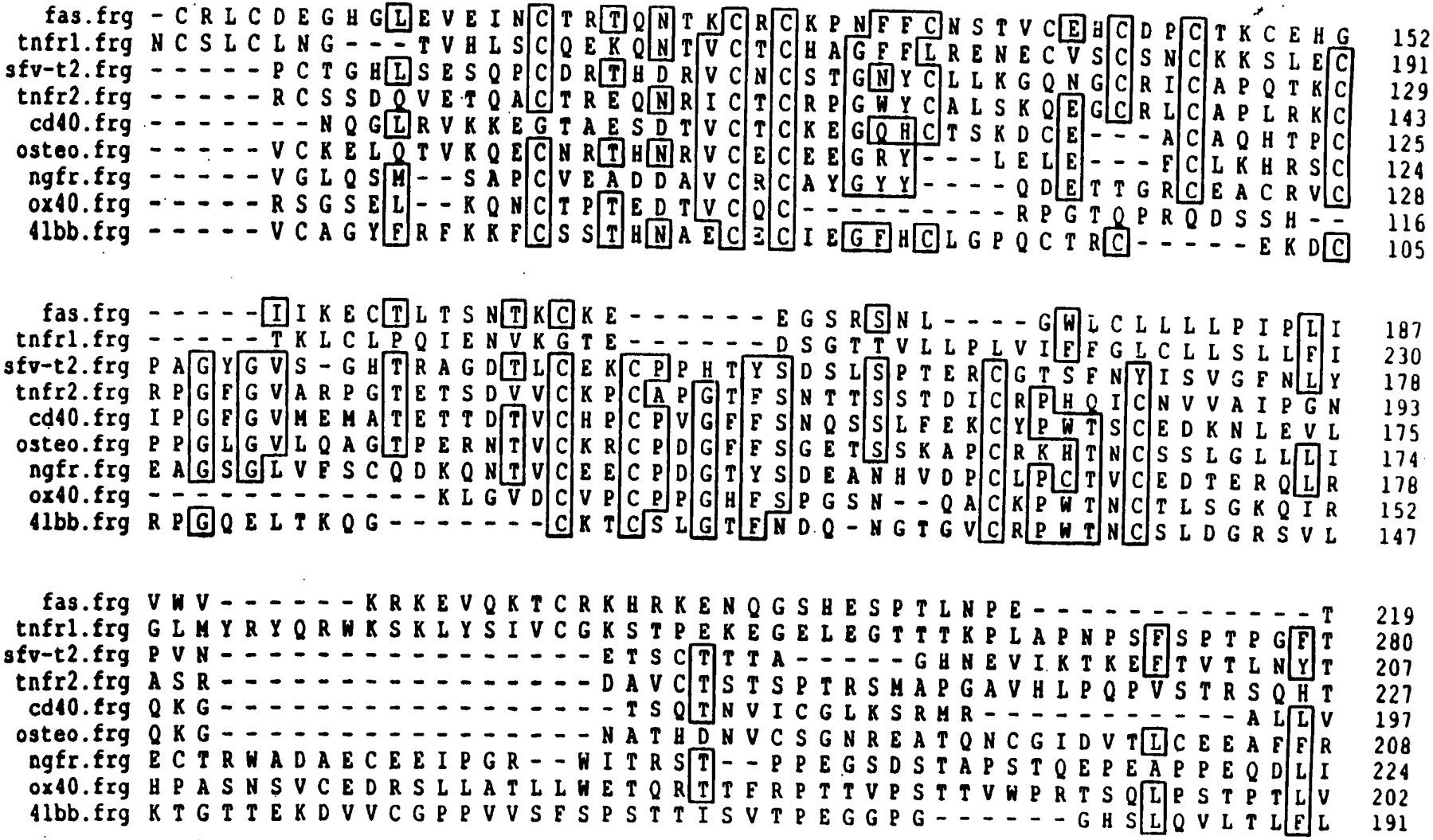


FIG.3A
FIG.3B
FIG.3C
FIG.3D
FIG.3E

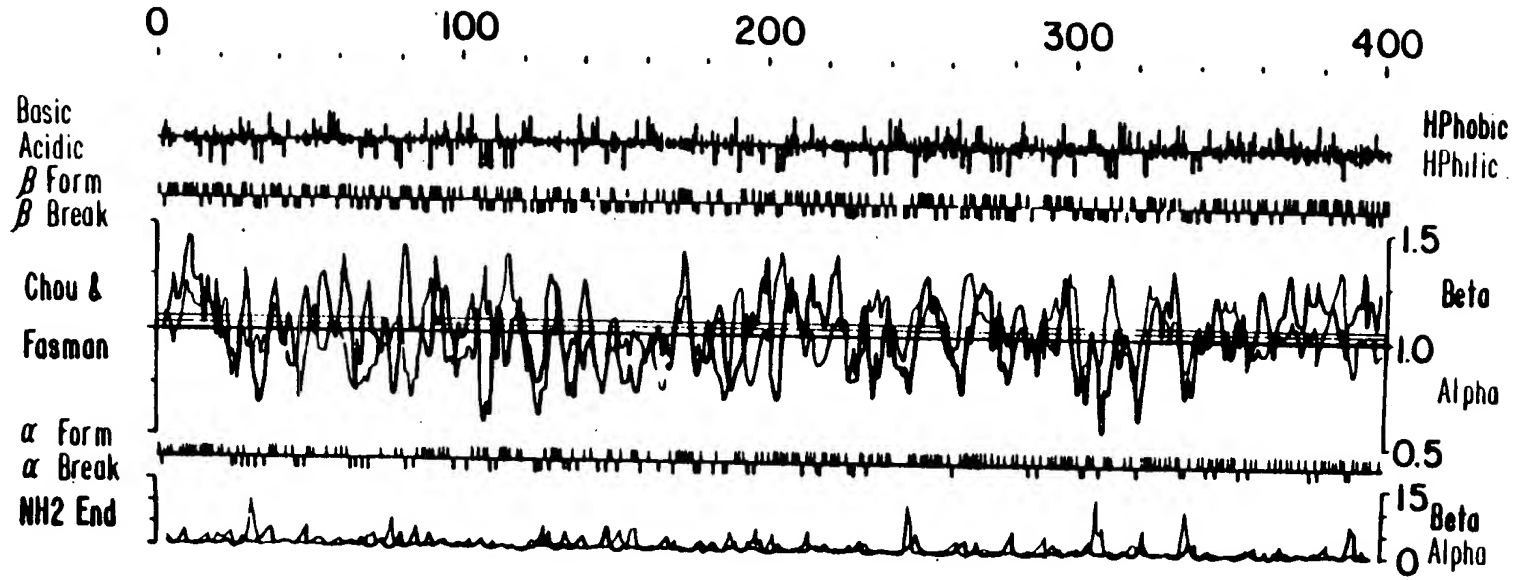


FIG.3F

FIG.3G

FIG.3H

FIG.3I

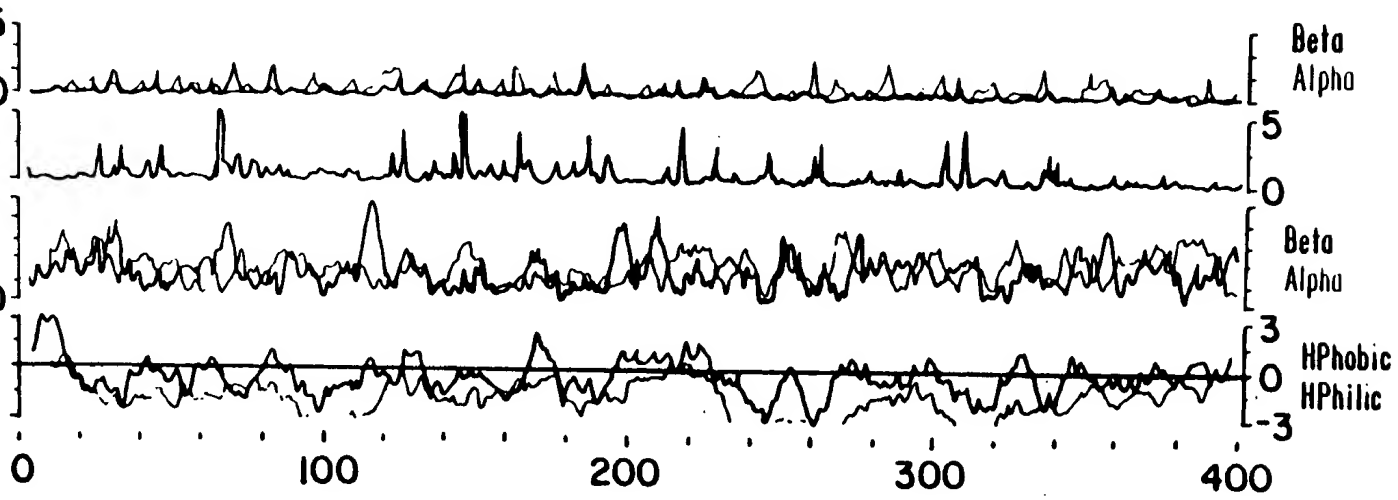


FIG.4A

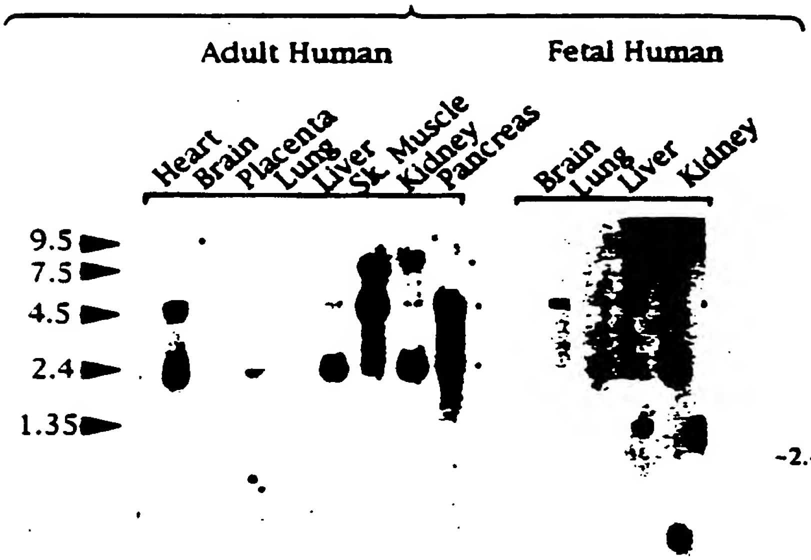


FIG.4B

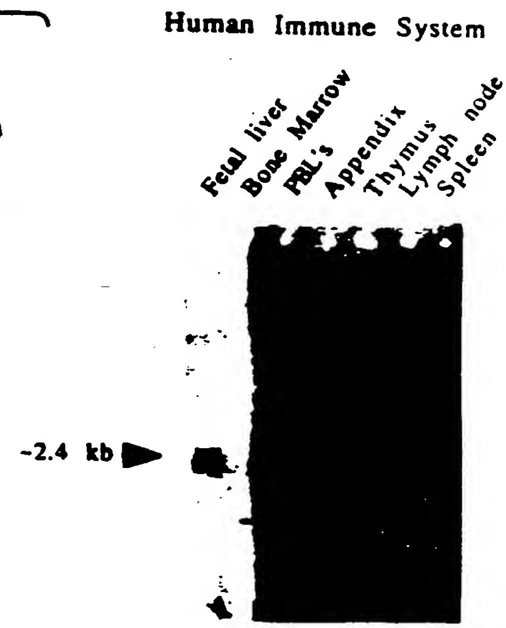


FIG.5

2 11 16 17 22 28 33 38 45 Kb 1 12 18 30

Transcgenic Founders Controls

FIG.6A

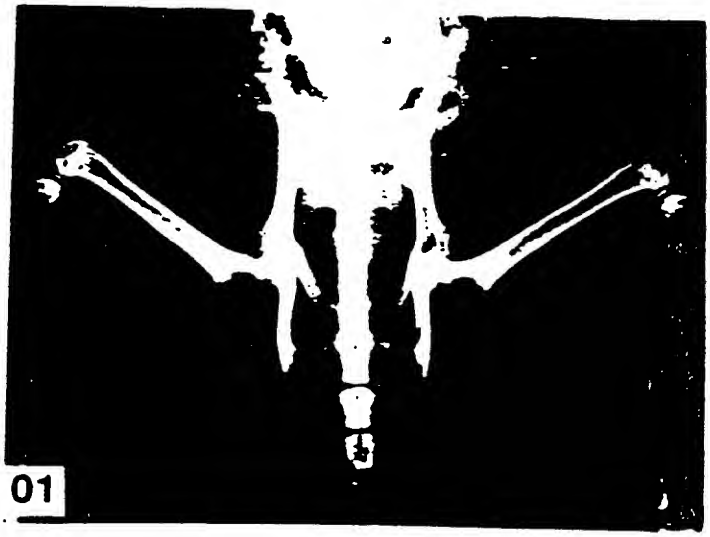


FIG.6B

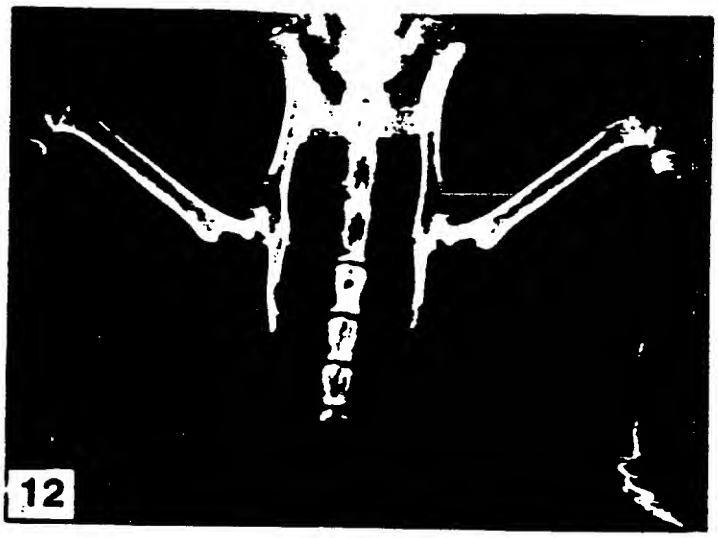


FIG.6C

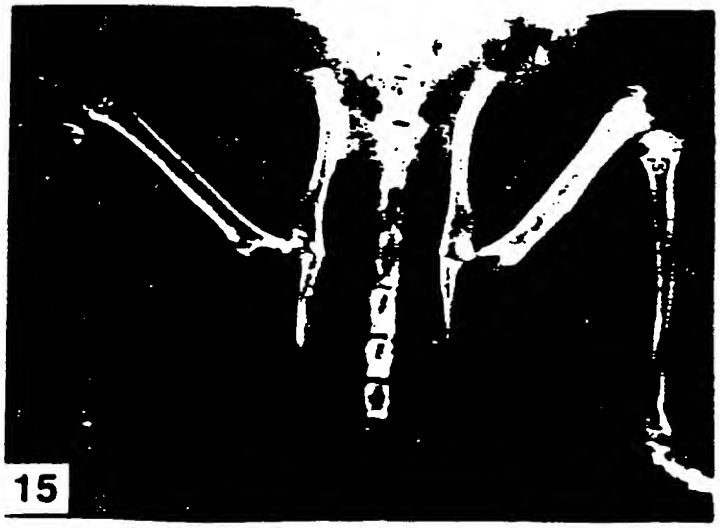


FIG.6D

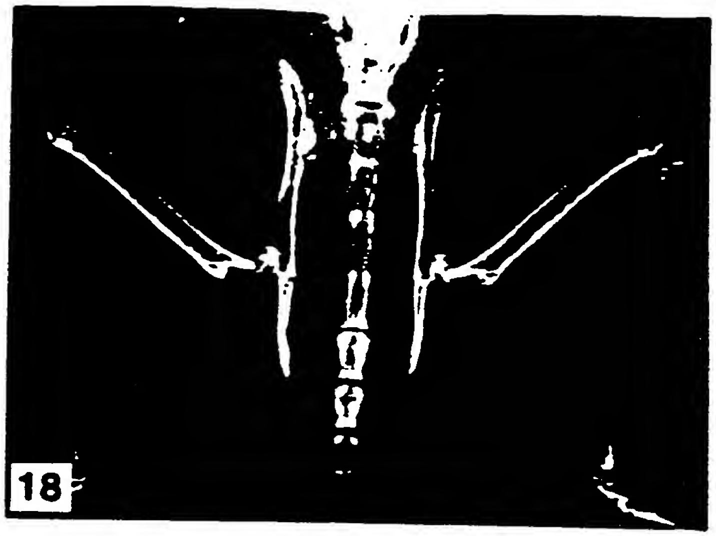


FIG.6E

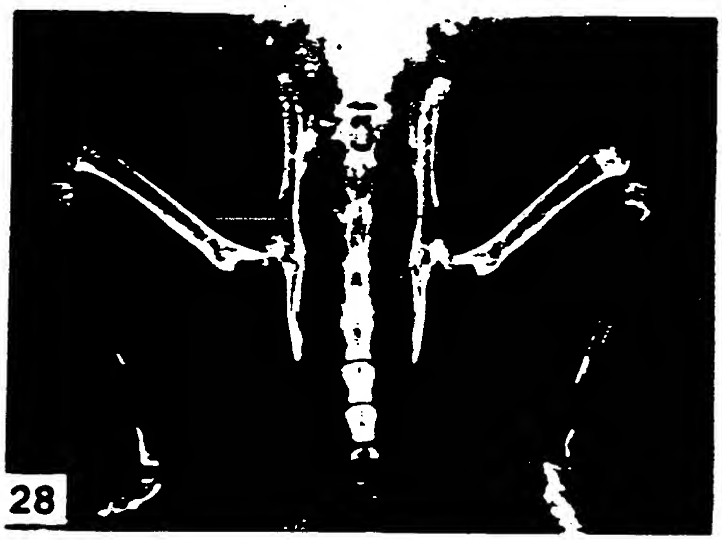


FIG.6F

FIG.6G

FIG.6H

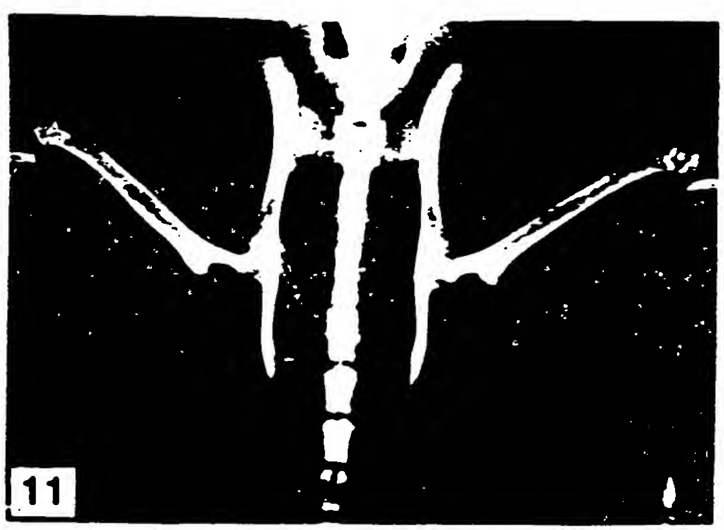


FIG.6I

FIG.6J

FIG.7A

FIG.7B

FIG.7C

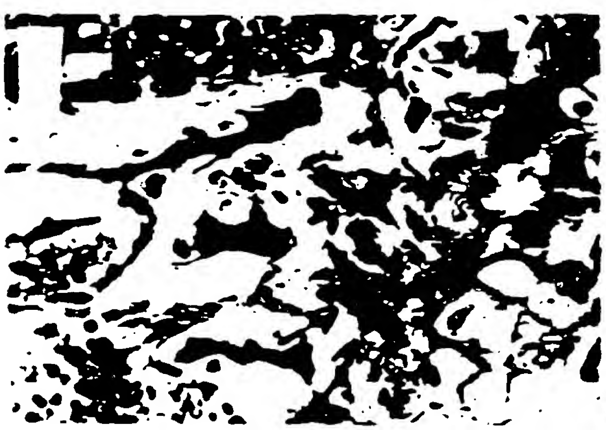


FIG.7D

FIG.7E

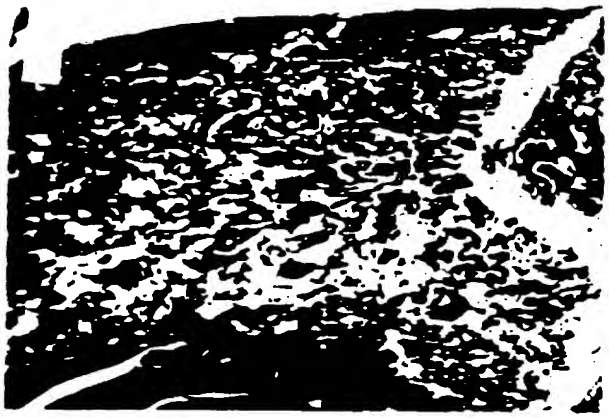


FIG.7F

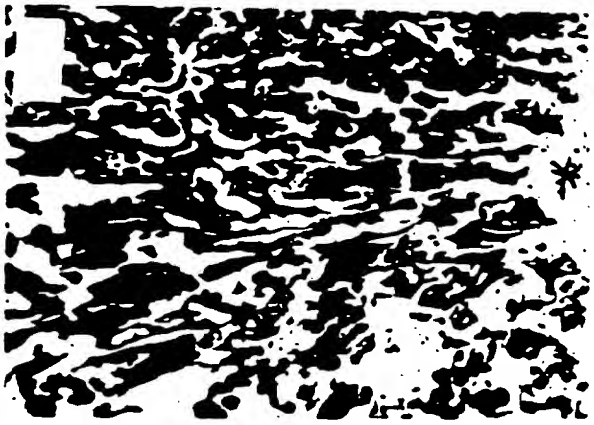


FIG.7G

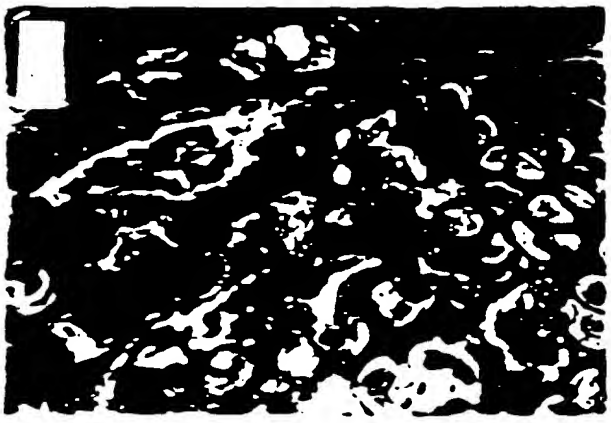


FIG.7H

FIG.8A

FIG.8B

FIG.8C

FIG.8D

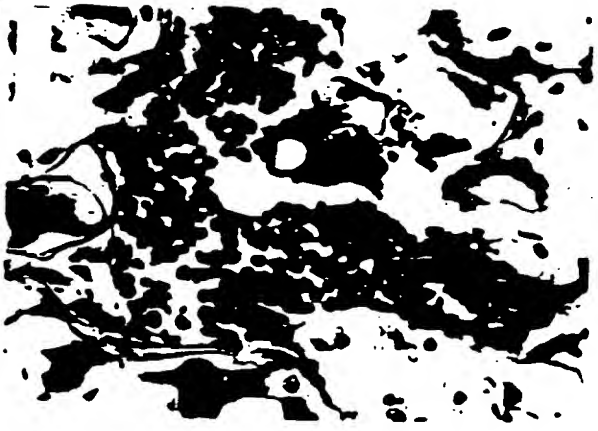


FIG.9A

10 30 50
CCTTATATAARACGTCATGATTGCCTGGGCTGCAGAGACGCACCTAGCACTGACCCAGCG
70 90 110
GCTGCCTCCTGAGGTTTCCCGAGGACCACAATGAACAAGTGGCTGTGCTGCGCACTCCTG
M N K W L C C A L L
130 150 170
GTGCTCCTGGACATCATTGAATGGACAACCCAGGAAACCCTTCCTCCAAAGTACTTGCAT
V L L D I I E W T T Q E T L P P K Y L H
190 210 230
TATGACCCAGAAACTGGTCATCAGCTCCTGTGTGACAAATGTGCTCCTGGCACCTACCTA
Y D P E T G H Q L L C D K C A P G T Y L
250 270 290
AAACAGCACTGCACAGTGAGGAGGAAGACATTGTGTGTCCCTTGCCCTGACCACTCTTAT
K Q H C T V R R K T L C V P C P D H S Y
310 330 350
ACGGACAGCTGGCACACCAGTGATGAGTGTGTGTATTGCAGCCCAGTGTGCAAGGAACTG
T D S W H T S D E C V Y C S P V C K E L
370 390 410
CAGTCCGTGAAGCAGGAGTGCAACCGCACCCACAACCGAGTGTGTGAGTGTGAGGAAGGG
Q S V K Q E C **N** R T H N R V C E C E E G
430 450 470
CGTTACCTGGAGATCGAATTCTGCTTGAAGCACCGGAGCTGTCCCCCGGGCTCCGGCGTG
R Y L E I E F C L K H R S C P P G S G V
490 510 530
GTGCAAGCTGGAACCCCAGAGCGAAACACAGTTTGCAAAAAATGTCCAGATGGGTTCTTC
V Q A G T P E R N T V C K K C P D G F F
550 570 590
TCAGGTGAGACTTCATCGAAAGCACCCTGTATAAAACACACGAACTGCAGCACATTTGGC
S G E T S S K A P C I K H T **N** C S T F G
610 630 650
CTCCTGCTAATTCAGAAAGGAAATGCAACACATGACAACGTGTGTTCCGGAAACAGAGAA
L L L I Q K G **N** A T H D N V C S G N R E
670 690 710
GCCACGCAAAAGTGTGGAATAGATGTCACCCTGTGTGAAGAGGCCTTCTTCAGGTTTGCT
A T Q K C G I D V T L C E E A F F R F A
730 750 770
GTTCCTACCAAGATTATACCAAATTGGCTGAGTGTTTTGGTGGACAGTTTGCCTGGGACC
V P T K I I P N W L S V L V D S L P G T

FIG.9B

```
        790                       810                       830
AAAGTGAATGCCGAGAGTGTAGAGAGGATAAAACGGAGACACAGCTCACAAGAGCAAACC
K  V  N  A  E  S  V  E  R  I  K  R  R  H  S  S  Q  E  Q  T
        850                       870                       890
TTCCAGCTGCTGAAGCTGTGGAAACATCAAAACAGAGACCAGGAAATGGTGAAGAAGATC
F  Q  L  L  K  L  W  K  H  Q  N  R  D  Q  E  M  V  K  K  I
        910                       930                       950
ATCCAAGACATTGACCTCTGTGAAAGCAGCGTGCAGCGGCATCTCGGCCACTCGAACCTC
I  Q  D  I  D  L  C  E  S  S  V  Q  R  H  L  G  H  S  N  L
        970                       990                      1010
ACCACAGAGCAGCTTCTTGCCTTGATGGAGAGCCTGCCTGGGAAGAAGATCAGCCCAGAA
T  T  E  Q  L  L  A  L  M  E  S  L  P  G  K  K  I  S  P  E
       1030                      1050                      1070
GAGATTGAGAGAACGAGAAAGACCTGCAAATCGAGCGAGCAGCTCCTGAAGCTACTCAGT
E  I  E  R  T  R  K  T  C  K  S  S  E  Q  L  L  K  L  L  S
       1090                      1110                      1130
TTATGGAGGATCAAAAATGGTGACCAAGACACCTTGAAGGGCCTGATGTATGCCCTCAAG
L  W  R  I  K  N  G  D  Q  D  T  L  K  G  L  M  Y  A  L  K
       1150                      1170                      1190
CACTTGAAAACATCCCACTTTCCCAAAACTGTCACCCACAGTCTGAGGAAGACCATGAGG
H  L  K  T  S  H  F  P  K  T  V  T  H  S  L  R  K  T  M  R
       1210                      1230                      1250
TTCCTGCACAGCTTCACAATGTACAGACTGTATCAGAAGCTCTTTTTAGAAATGATAGGG
F  L  H  S  F  T  M  Y  R  L  Y  Q  K  L  F  L  E  M  I  G
       1270                      1290                      1310
AATCAGGTTCAATCCGTGAAAATAAGCTGCTTATAACTAGGAATGGTCACTGGGCTGTTT
N  Q  V  Q  S  V  K  I  S  C  L

CTTCA
```

FIG.9C

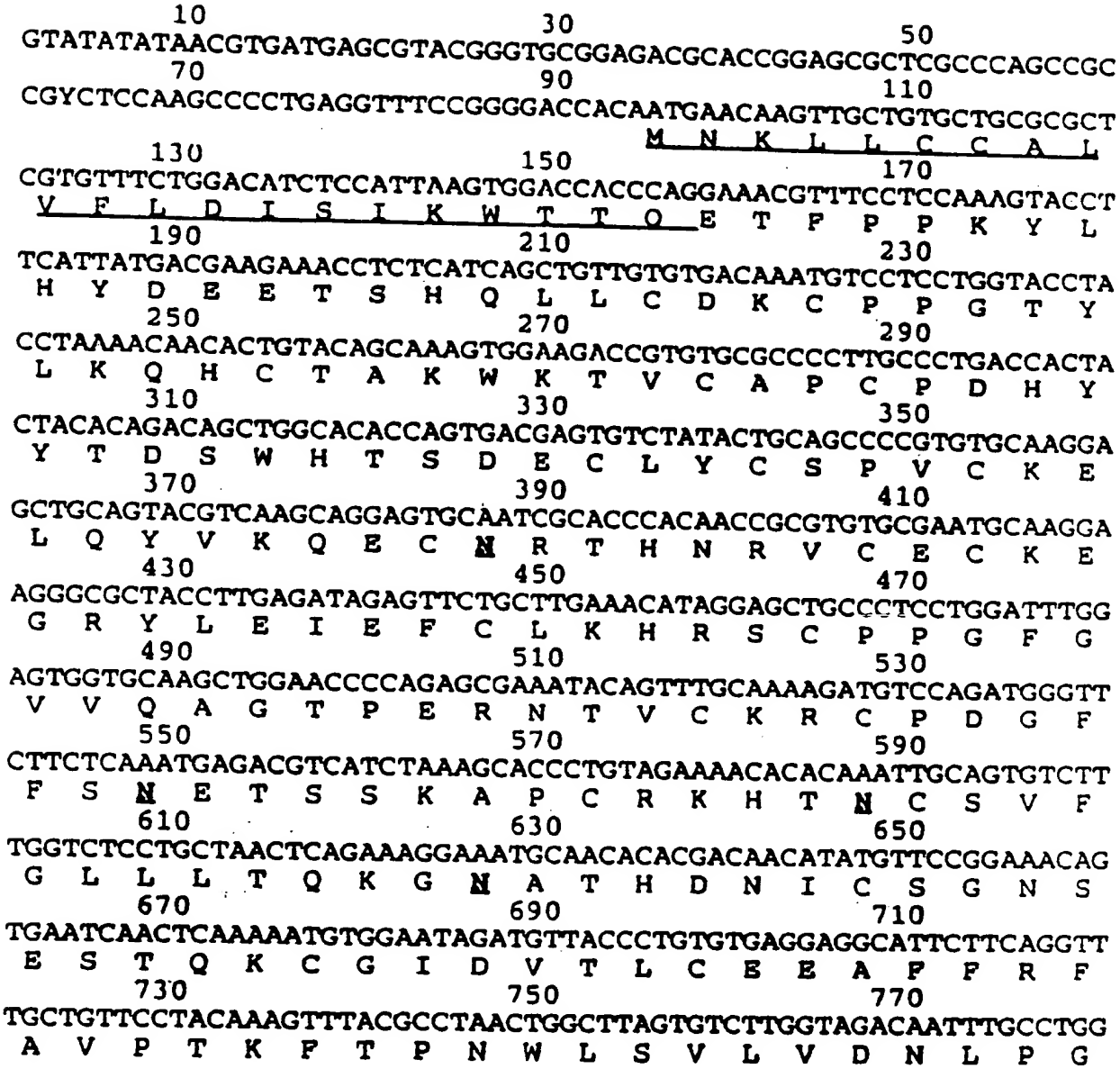


FIG.9D

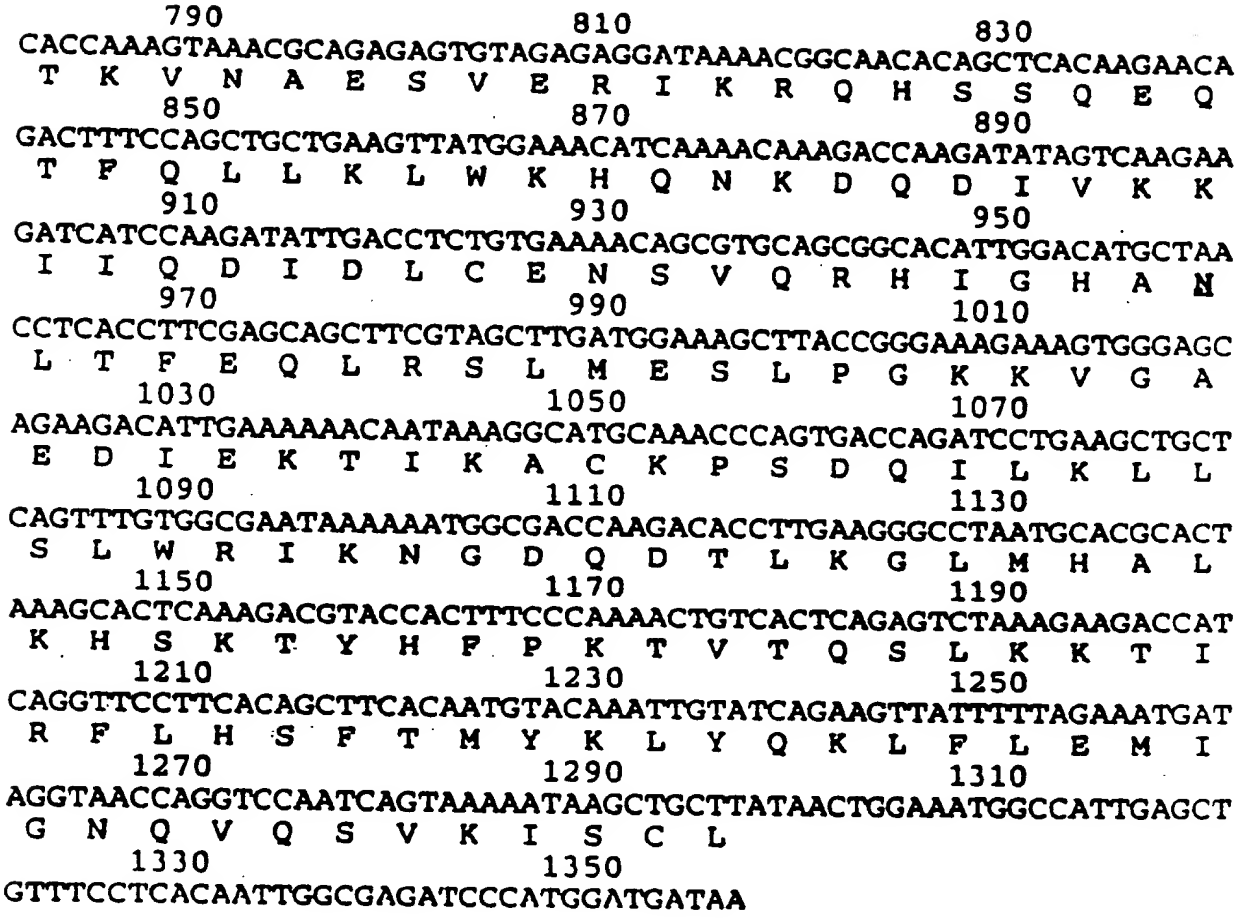

790
810
830
CACCAAAGTAAACGCAGAGAGTGTAGAGAGGATAAAACGGCAACACAGCTCACAAGAACA
T K V N A E S V E R I K R Q H S S Q E Q
850
870
890
GACTTTCCAGCTGCTGAAGTTATGGAAACATCAAAACAAAGACCAAGATATAGTCAAGAA
T F Q L L K L W K H Q N K D Q D I V K K
910
930
950
GATCATCCAAGATATTGACCTCTGTGAAAACAGCGTGCAGCGGCACATTGGACATGCTAA
I I Q D I D L C E N S V Q R H I G H A N
970
990
1010
CCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAAAGCTTACCGGGAAAGAAAGTGGGAGC
L T F E Q L R S L M E S L P G K K V G A
1030
1050
1070
AGAAGACATTGAAAAAACAATAAAGGCATGCAAACCCAGTGACCAGATCCTGAAGCTGCT
E D I E K T I K A C K P S D Q I L K L L
1090
1110
1130
CAGTTTGTGGCGAATAAAAAATGGCGACCAAGACACCTTGAAGGGCCTAATGCACGCACT
S L W R I K N G D Q D T L K G L M H A L
1150
1170
1190
AAAGCACTCAAAGACGTACCACTTTCCCAAAACTGTCACTCAGAGTCTAAAGAAGACCAT
K H S K T Y H F P K T V T Q S L K K T I
1210
1230
1250
CAGGTTCCTTCACAGCTTCACAATGTACAAATTGTATCAGAAGTTATTTTTAGAAATGAT
R F L H S F T M Y K L Y Q K L F L E M I
1270
1290
1310
AGGTAACCAGGTCCAATCAGTAAAAATAAGCTGCTTATAACTGGAAATGGCCATTGAGCT
G N Q V Q S V K I S C L
1330
1350
GTTTCCTCACAATTGGCGAGATCCCATGGATGATAA

FIG.9E

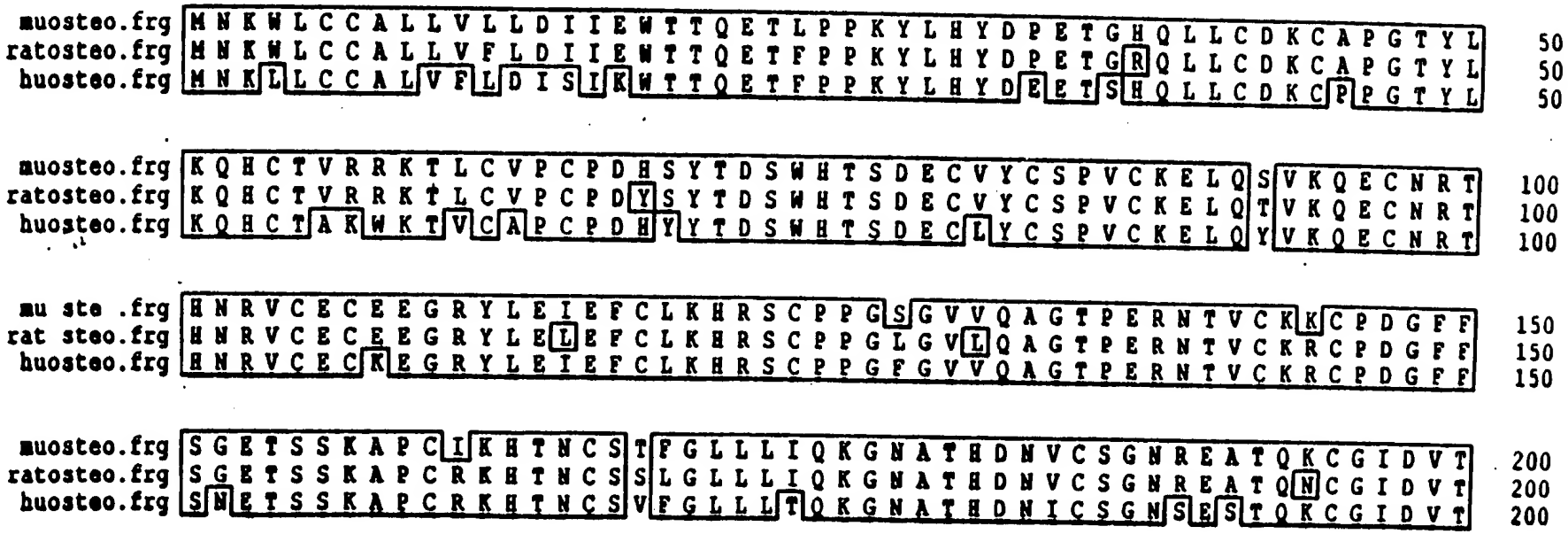


FIG.9F

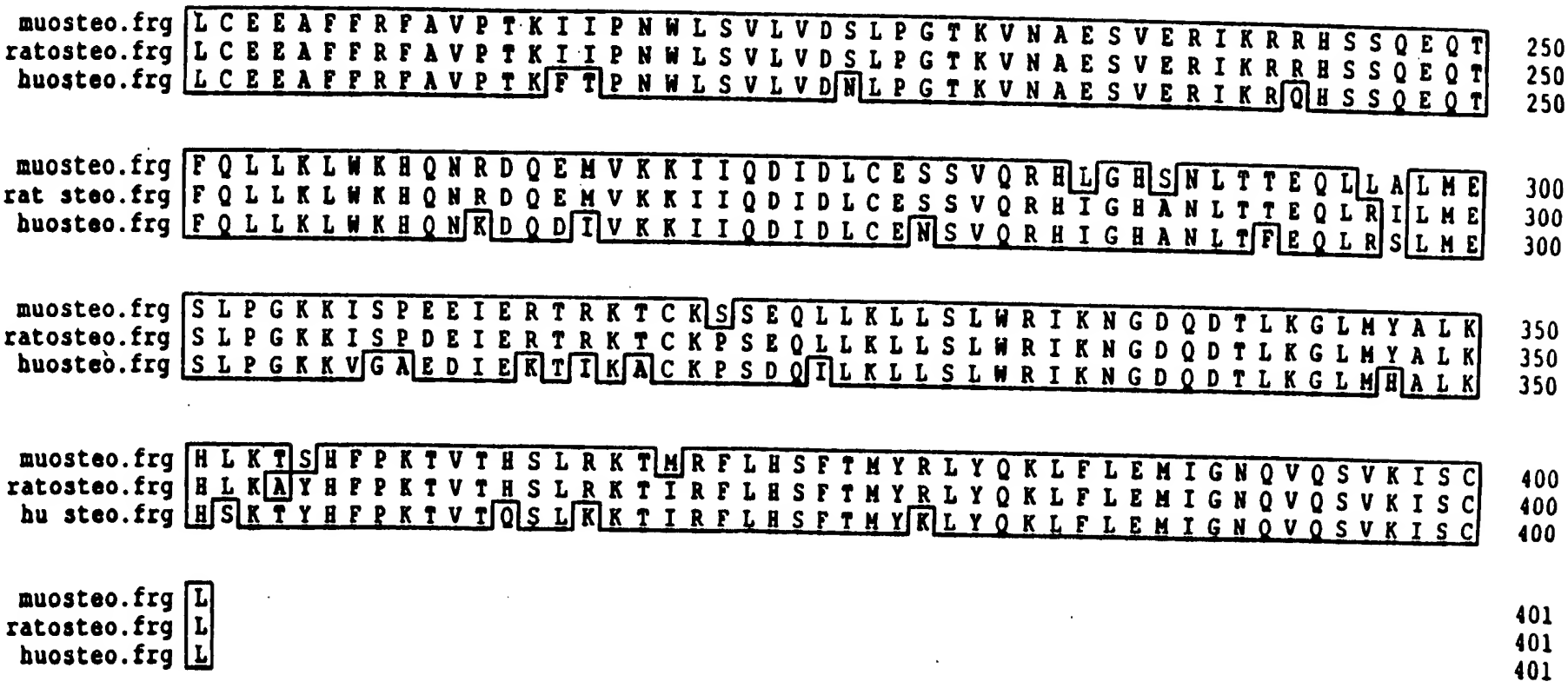


FIG.10

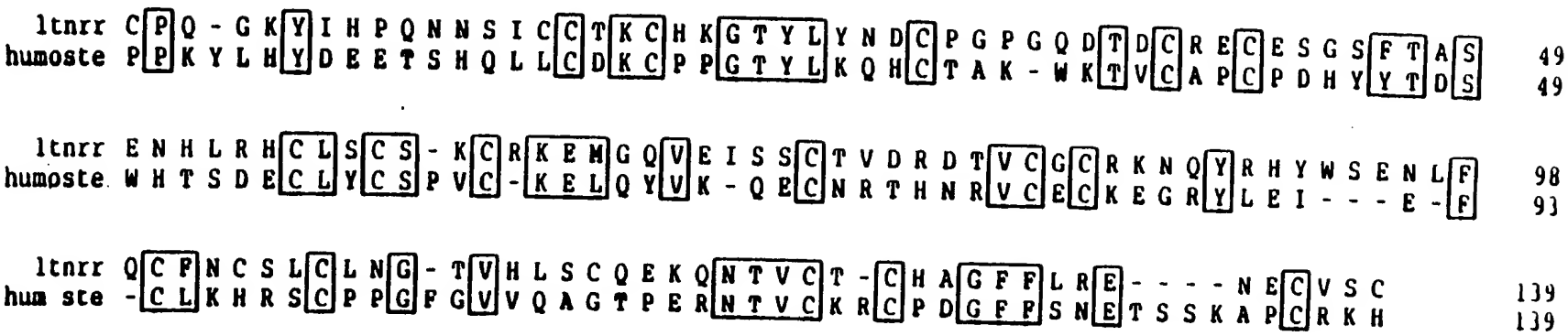

ltnrr C P Q - G K Y I H P Q N N S I C C T K C H K G T Y L Y N D C P G P G Q D T D C R E C E S G S F T A S 49
humoste P P K Y L H Y D E E T S H Q L L C D K C P P G T Y L K Q H C T A K - W K T V C A P C P D H Y Y T D S 49
ltnrr E N H L R H C L S C S - K C R K E M G Q V E I S S C T V D R D T V C G C R K N Q Y R H Y W S E N L F 98
humoste W H T S D E C L Y C S P V C - K E L Q Y V K - Q E C N R T H N R V C E C K E G R Y L E I - - - E - F 93
ltnrr Q C F N C S L C L N G - T V H L S C Q E K Q N T V C T - C H A G F F L R E - - - - N E C V S C 139
hum ste - C L K H R S C P P G F G V V Q A G T P E R N T V C K R C P D G F F S N E T S S K A P C R K H 139

FIG. 11

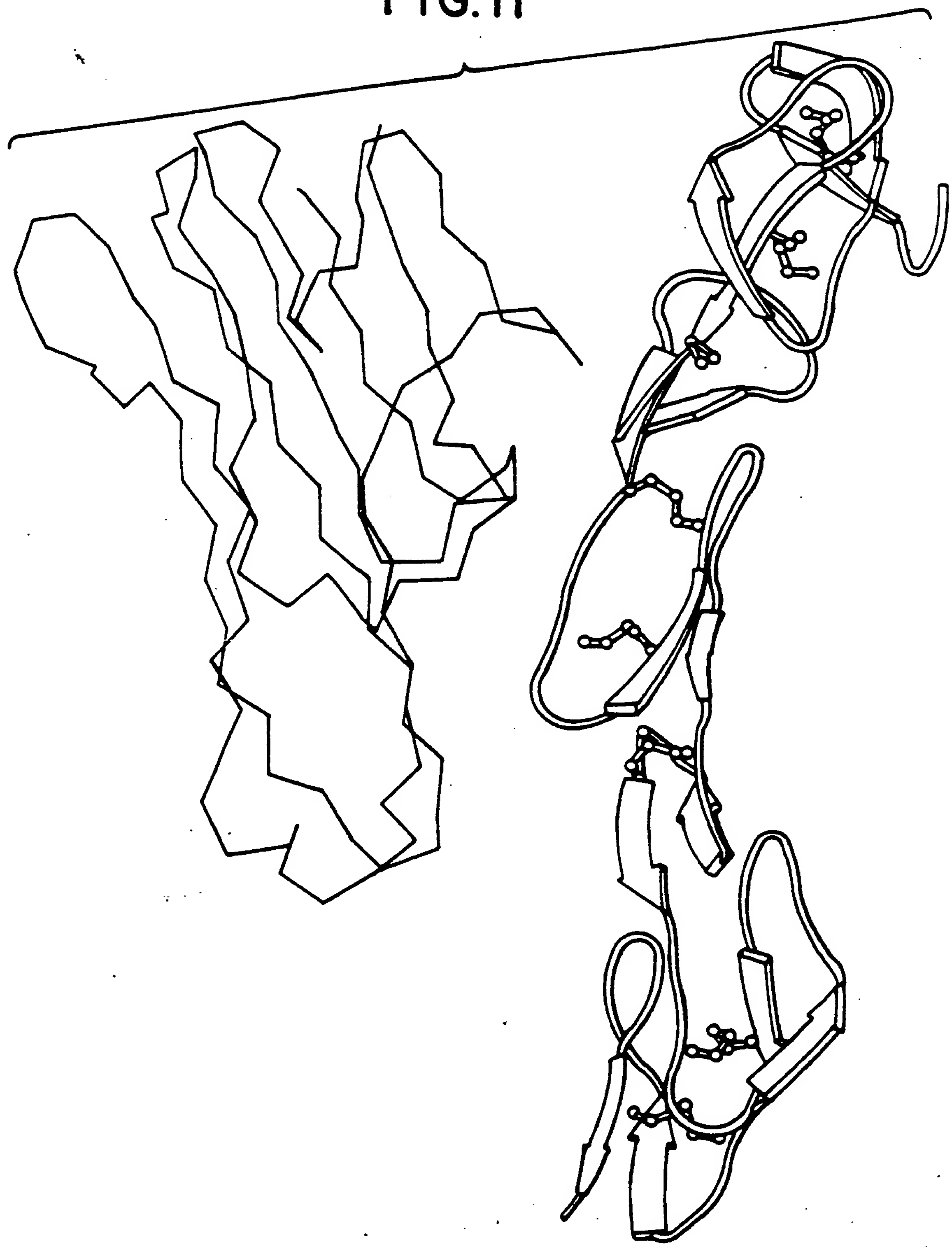


FIG.12A

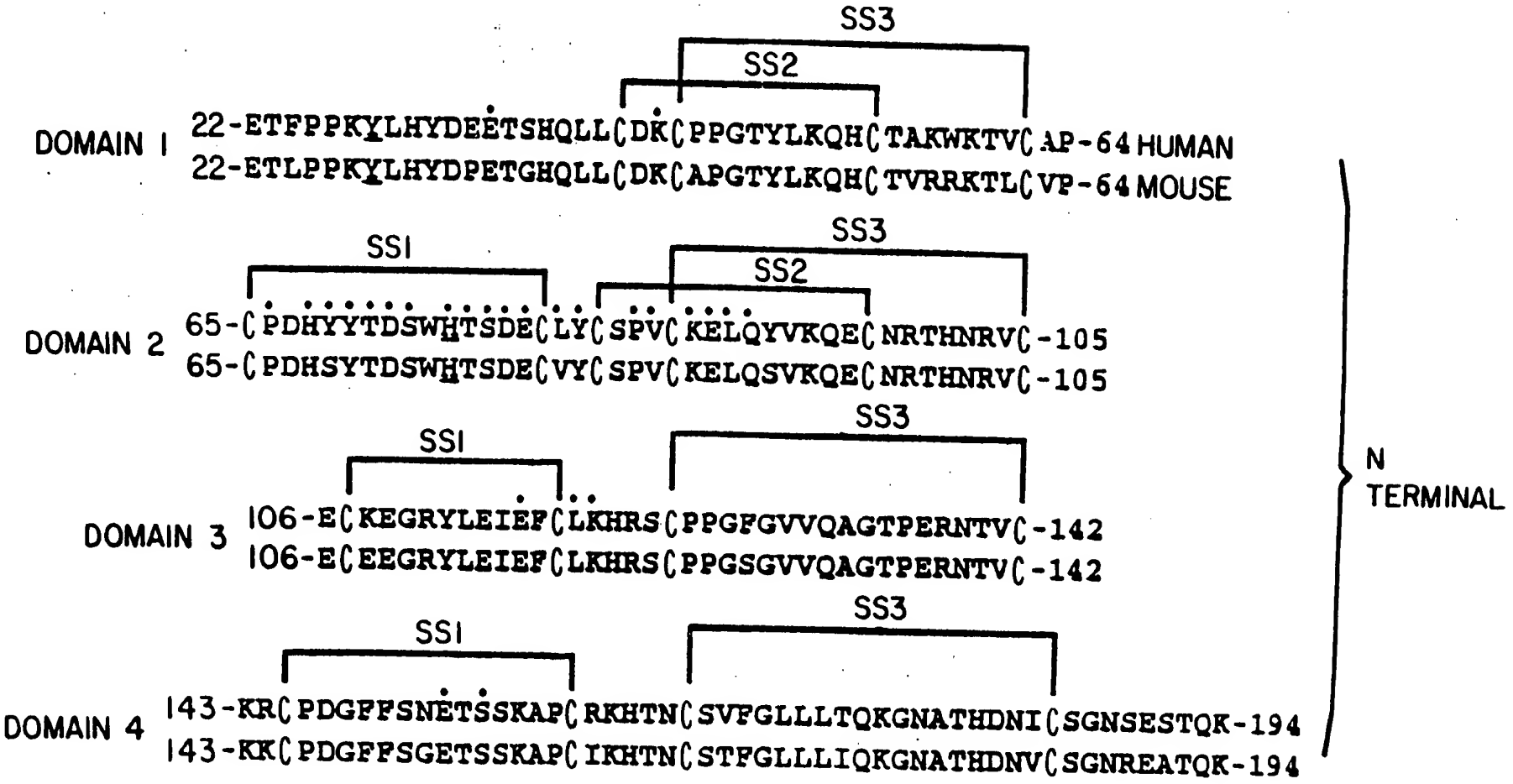


FIG.12B

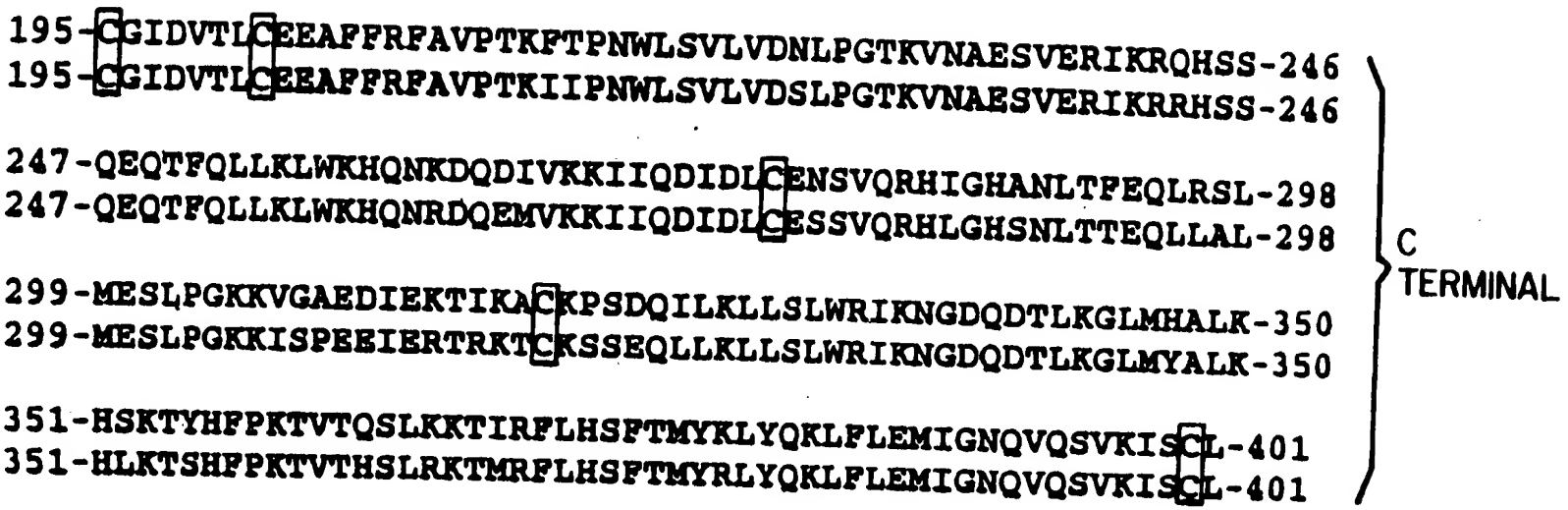


FIG.13A

FIG.13B

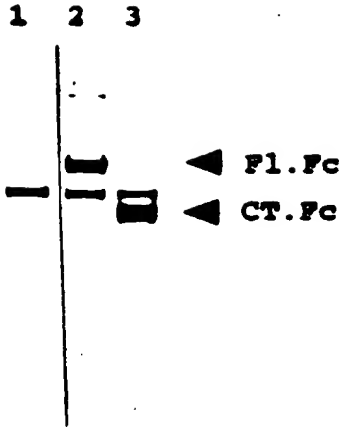


FIG.13C

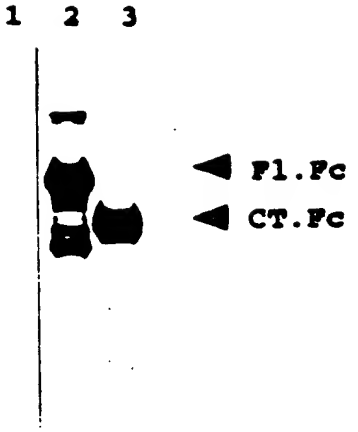


FIG.14A

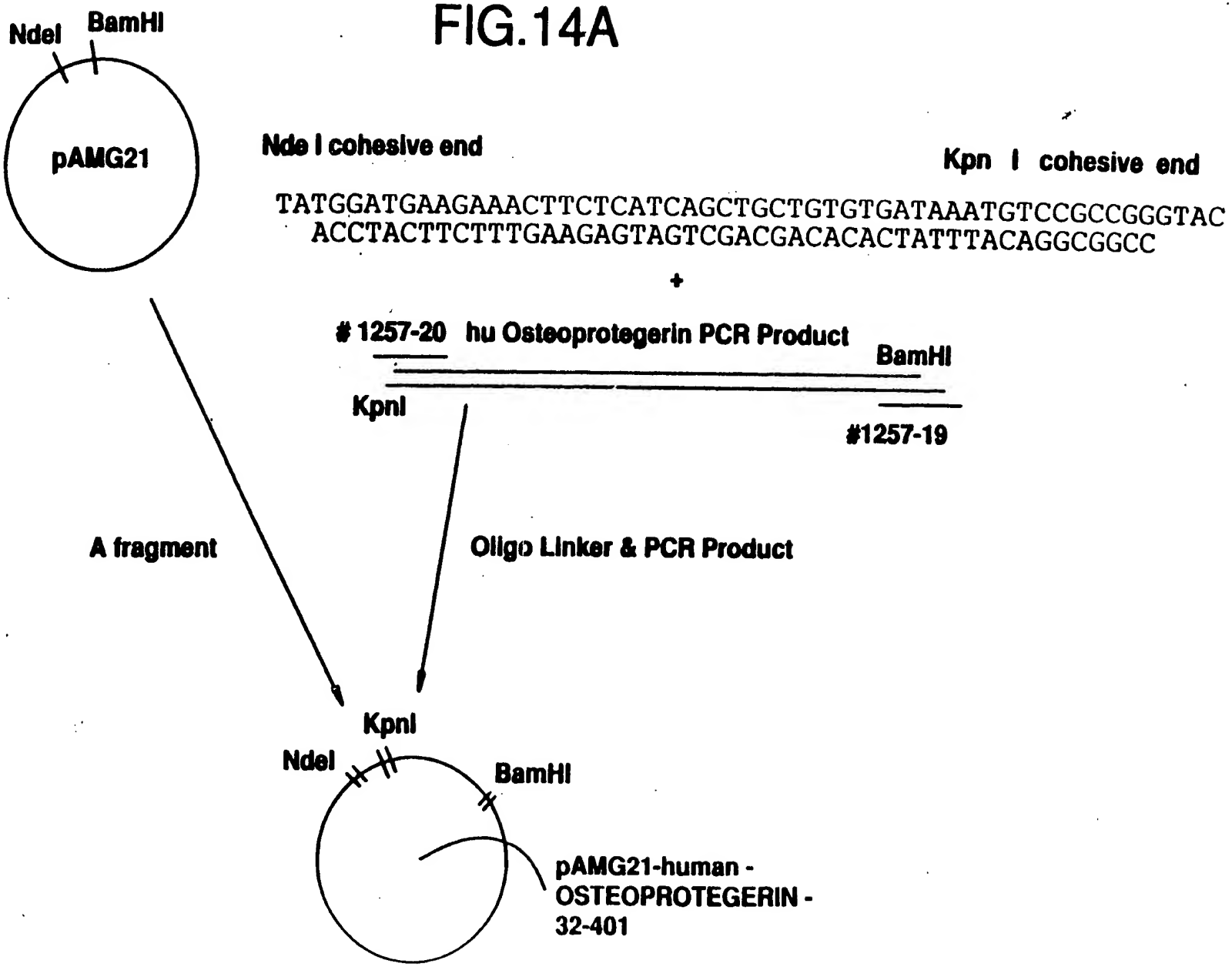


FIG.14B

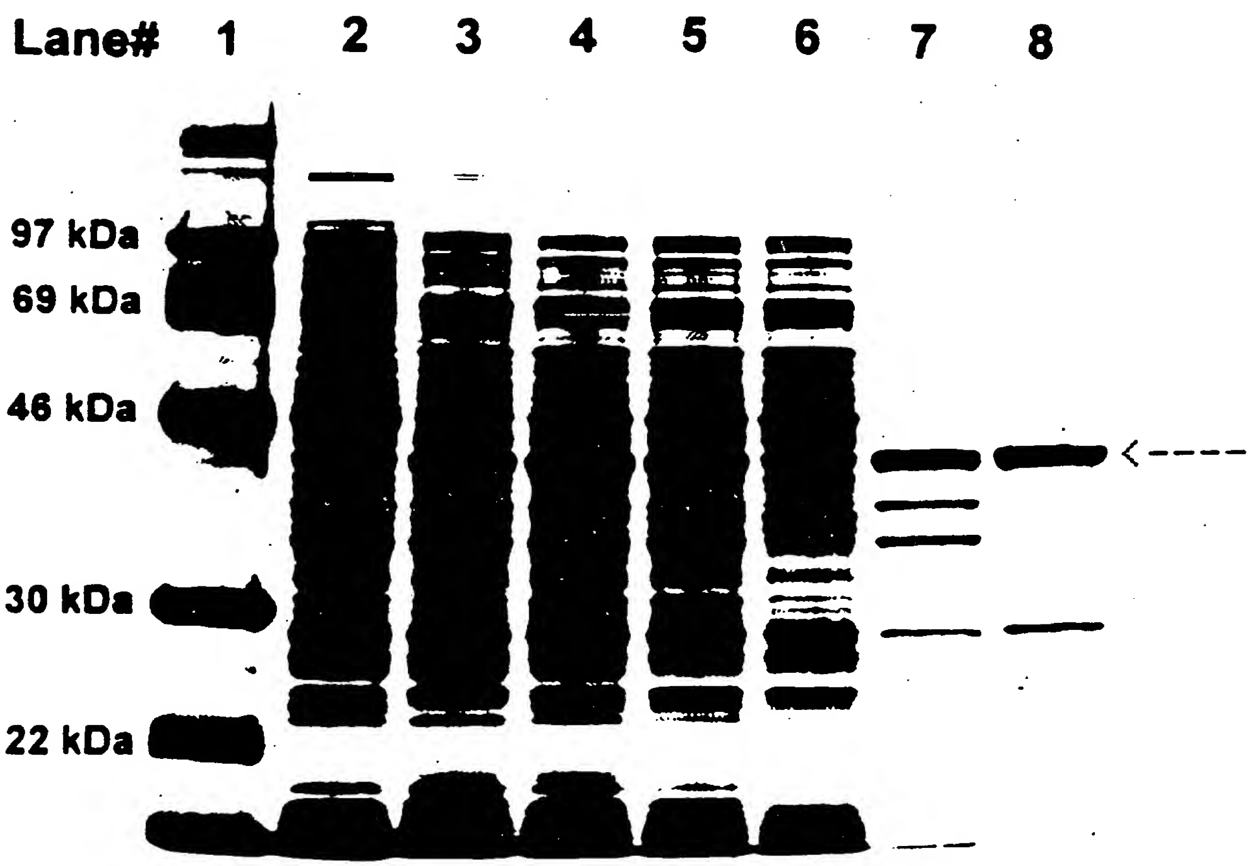


FIG.15

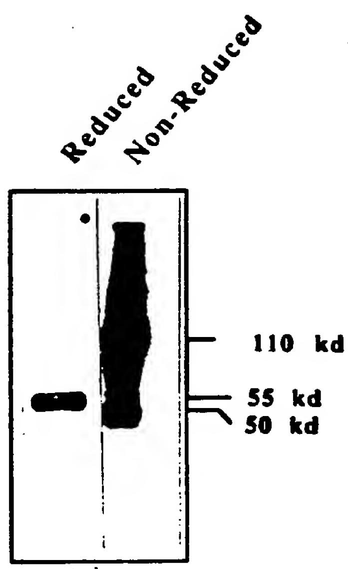


FIG. 16A

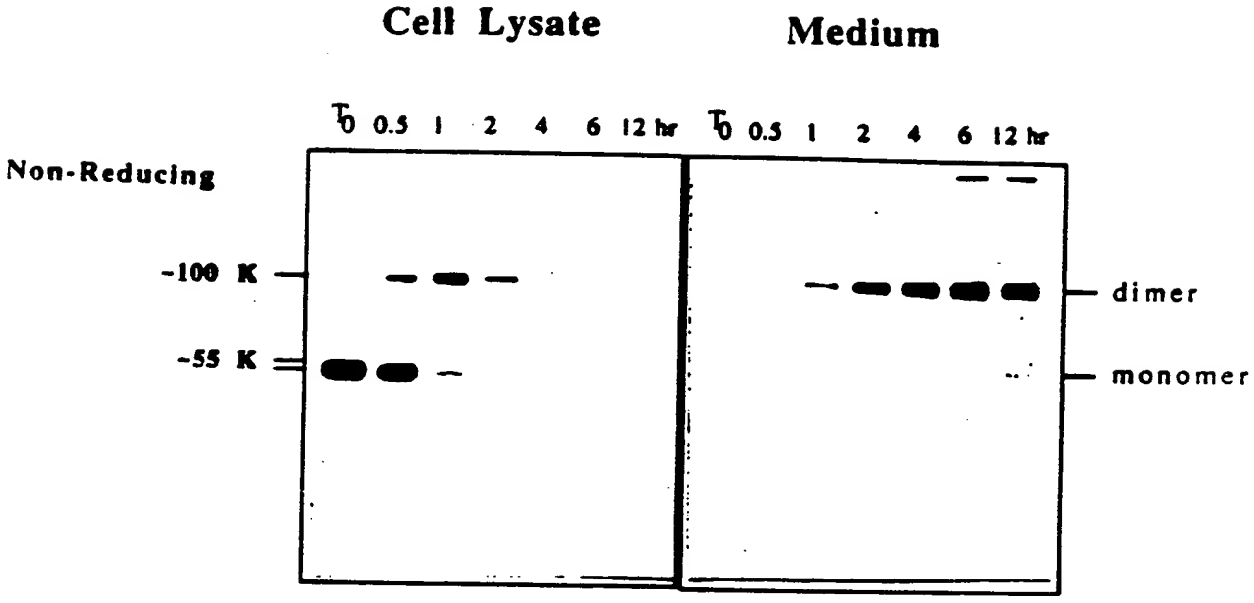


FIG. 16B

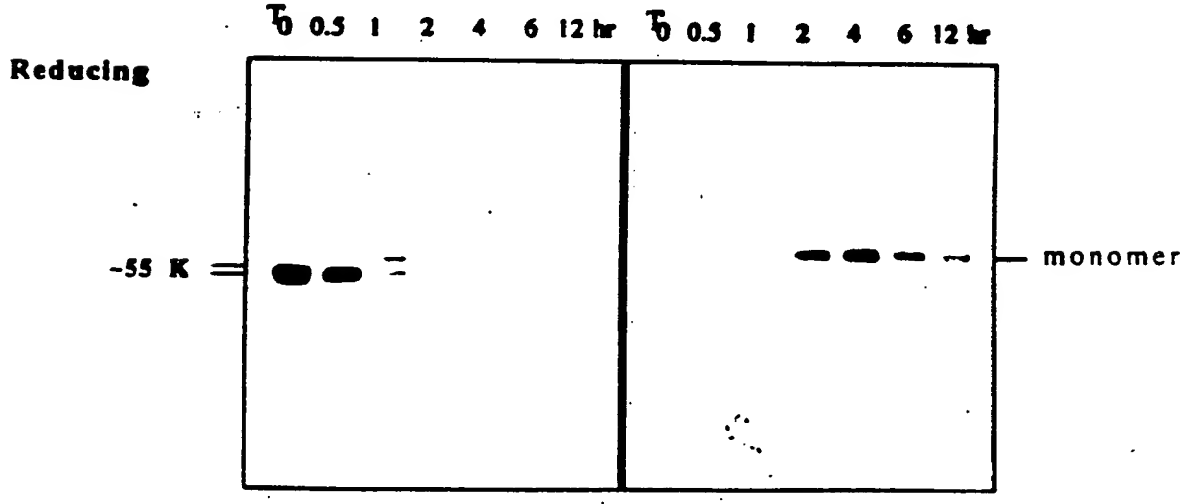


FIG. 17

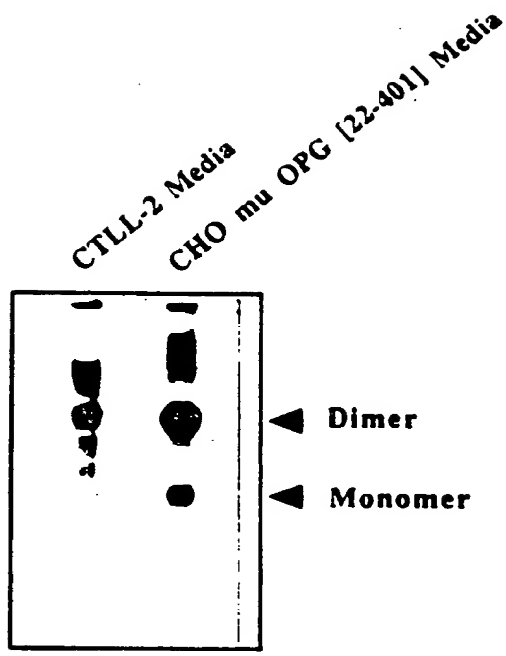


FIG.18

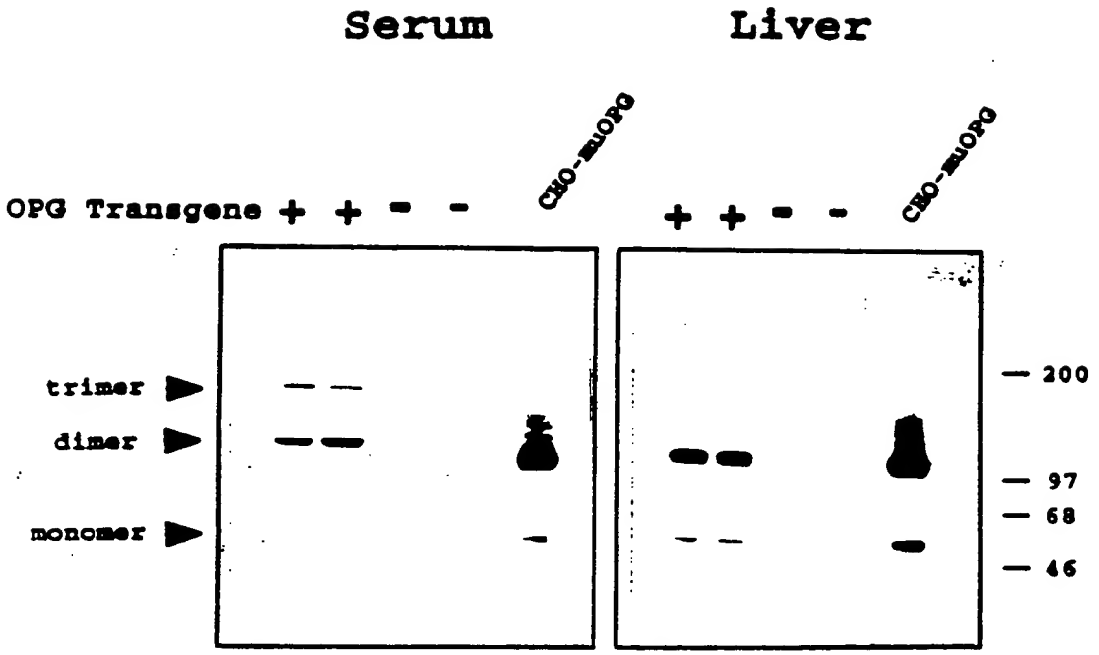

Serum
Liver
OPG Transgene + + - - CHO-mOPG
+ + - - CHO-mOPG
trimer
dimer
monomer
200
97
68
46

FIG.19A

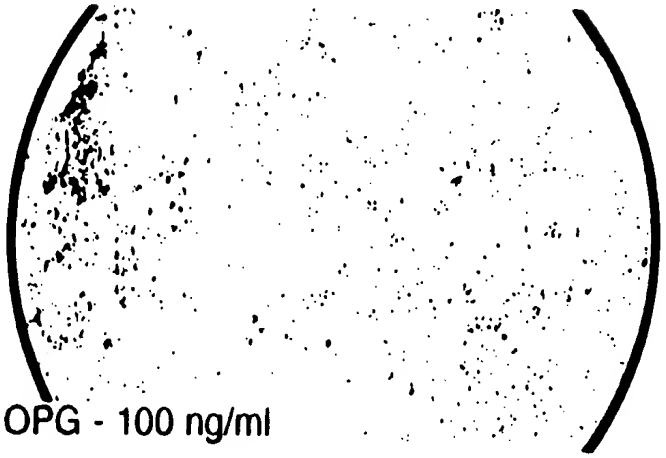


FIG.19B

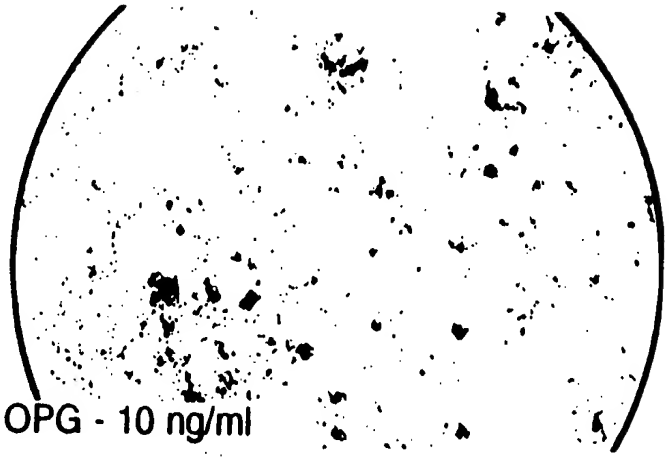


FIG.19C

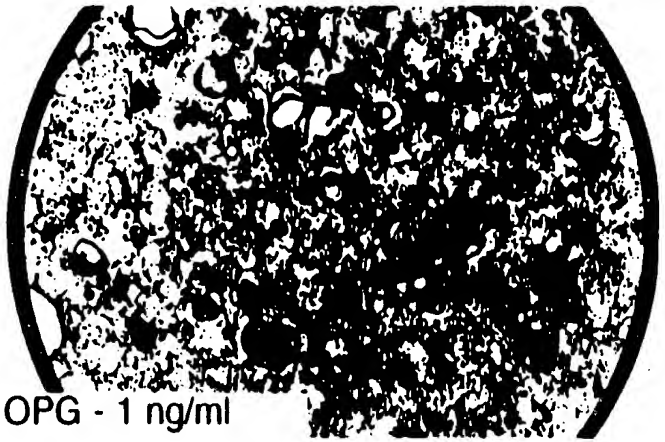


FIG.19D

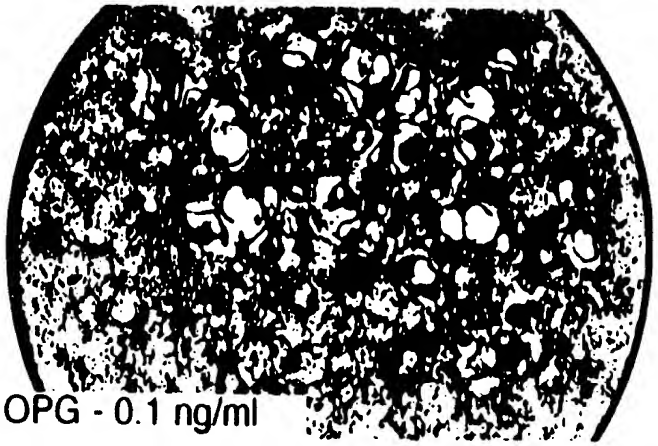
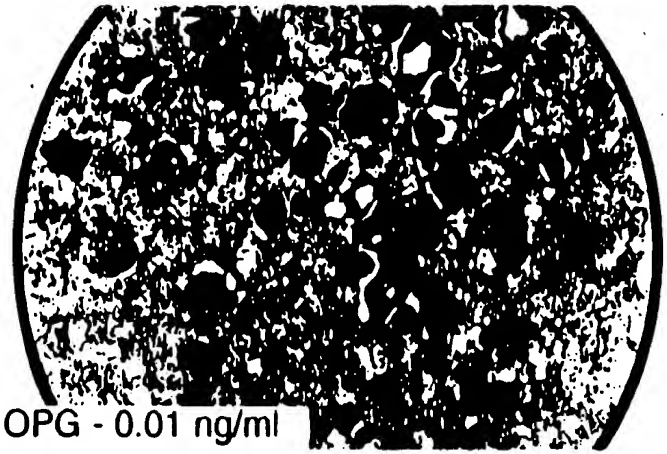
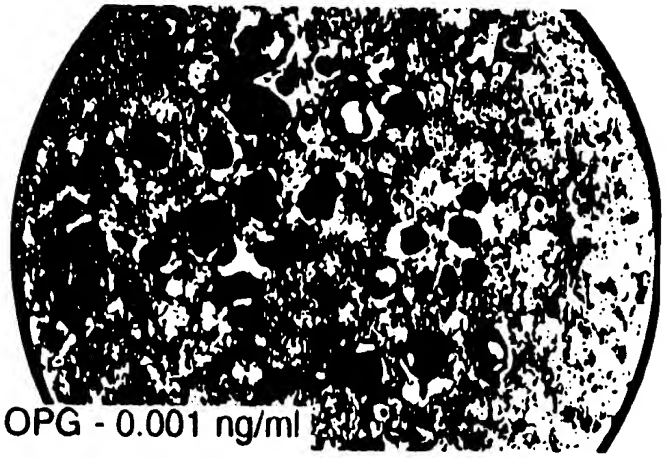


FIG.19E



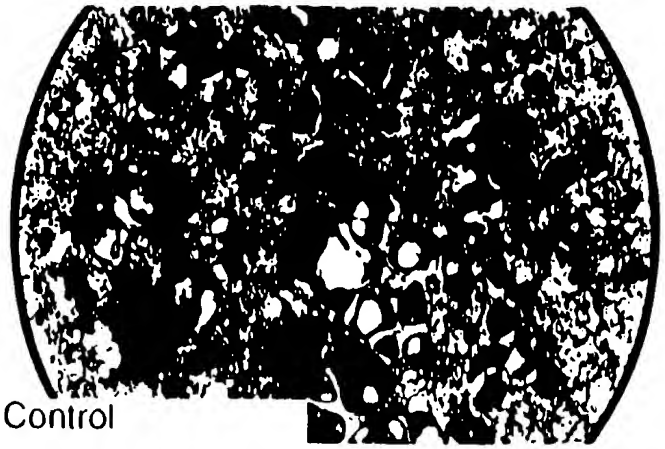
OPG - 0.01 ng/ml

FIG.19F



OPG - 0.001 ng/ml

FIG.19G



Control

FIG.20

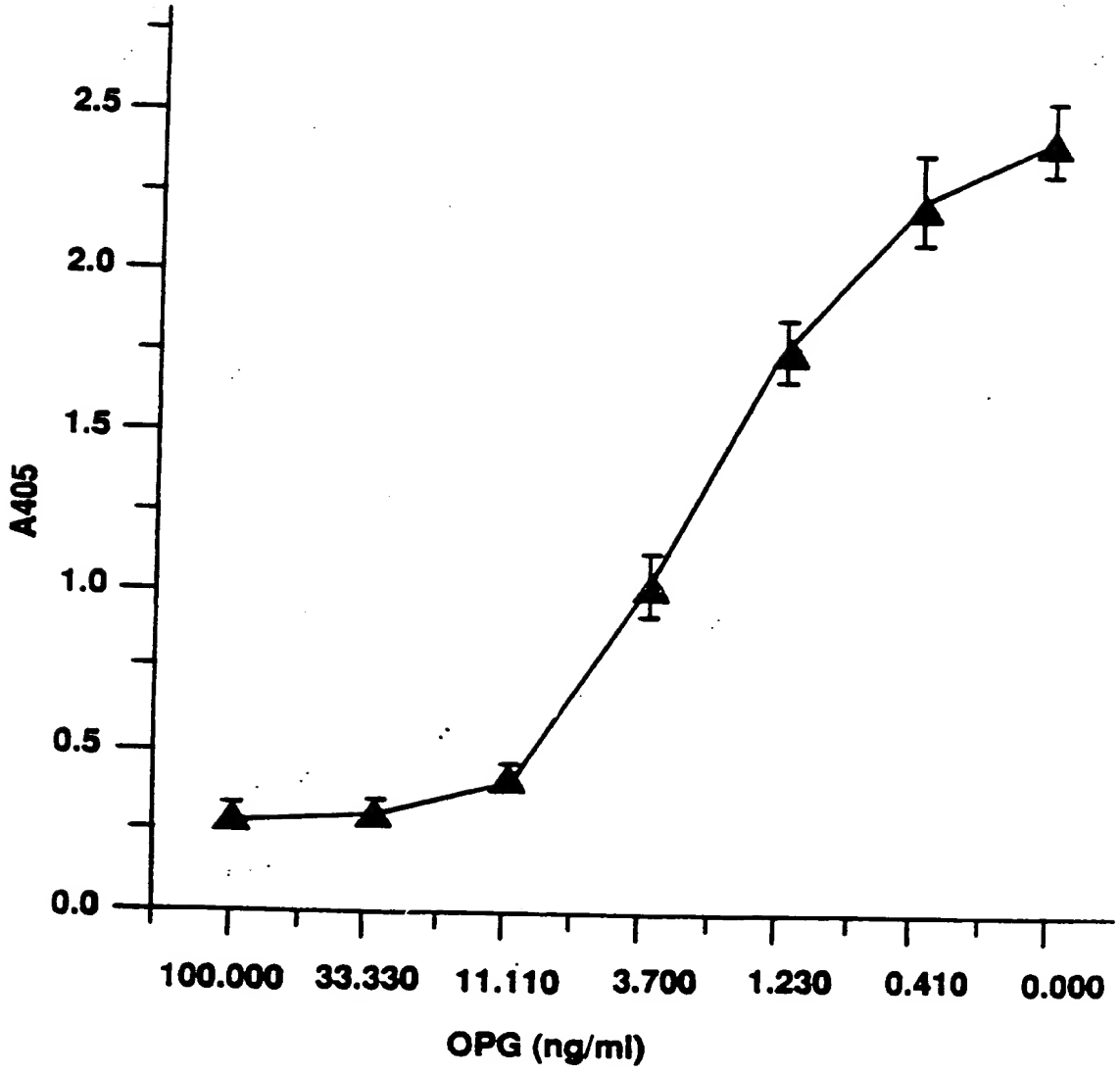
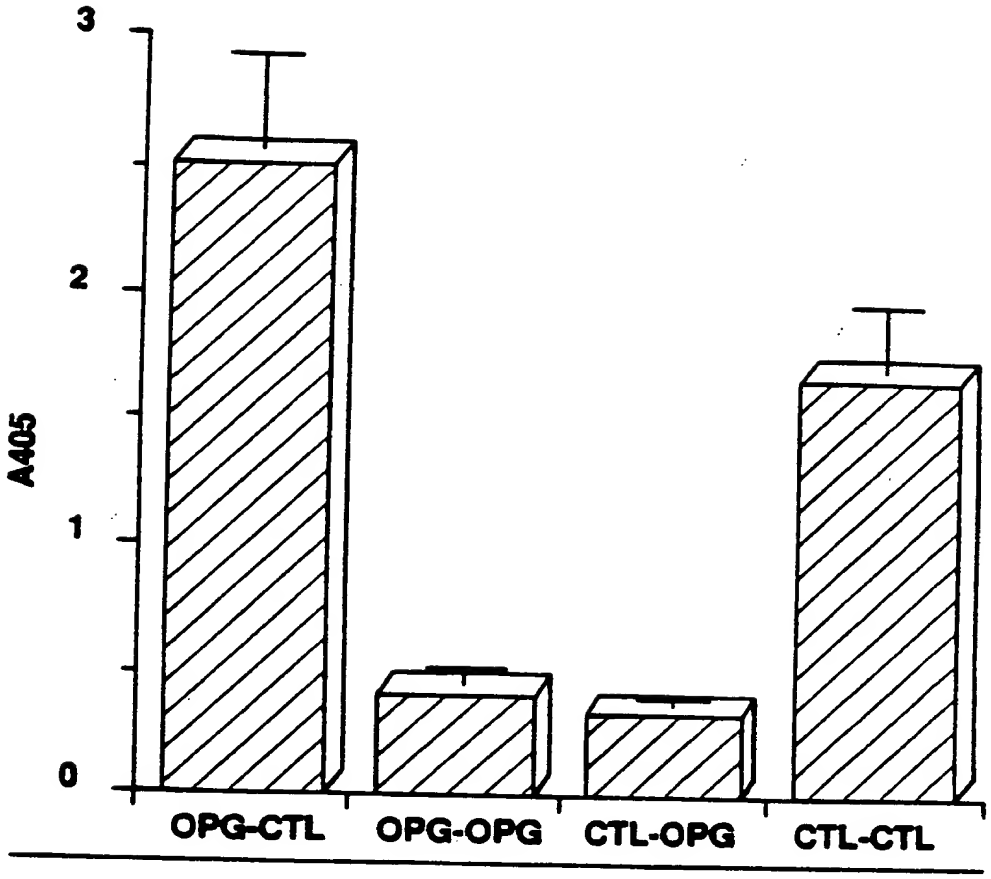

2.5
2.0
1.5
1.0
0.5
0.0
A405
100.000
33.330
11.110
3.700
1.230
0.410
0.000
OPG (ng/ml)

FIG.21



Legend

Growth	Intermediate	Terminal
Bone marrow cells	PGE2 + CSF-1	ST2 cells
CSF -1		1,25 (OH)2 D3
		Dexamethasone
4 days	2 days	8 - 10 days

Groups	OPG	OPG
CTL - CTL	– – –	– – –
OPG - CTL	100 ng/ml	– – –
OPG - OPG	– – –	100 ng/ml
OPG - OPG	100 ng/ml	100 ng/ml

FIG.22A

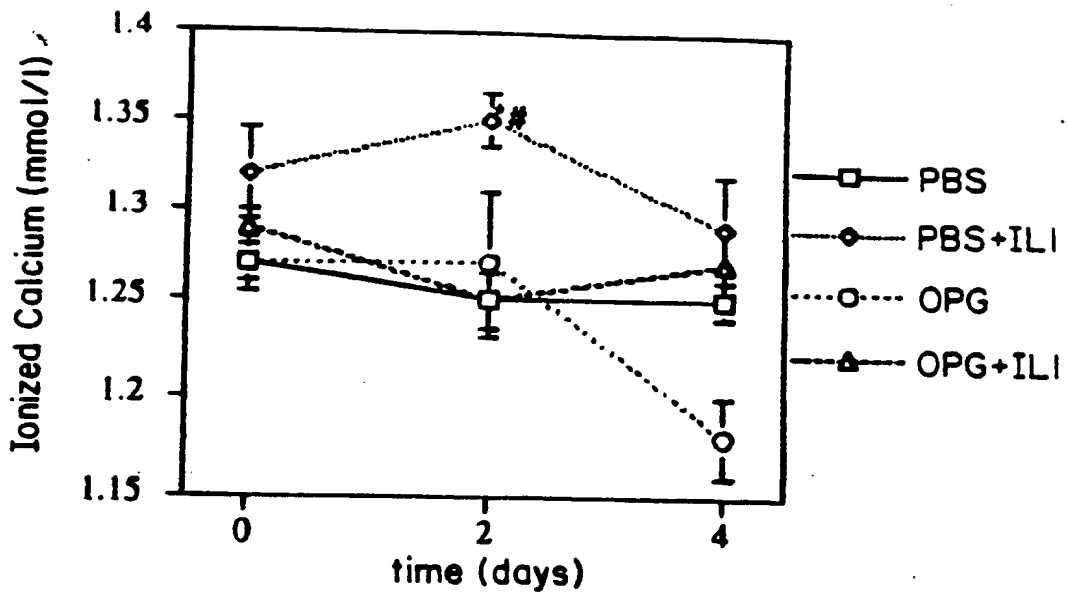
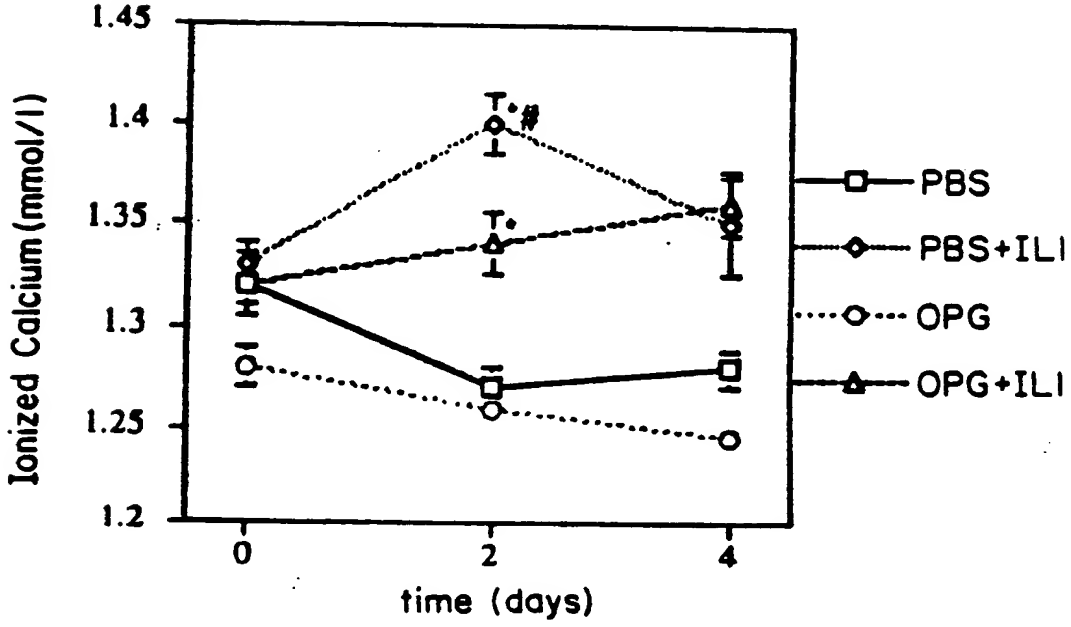


FIG.22B



* Different to PBS, $p < 0.05$
# Different to OPG + IL1, $p < 0.05$

FIG.23A

PBS/PBS

FIG.23B

FIG.23C

FIG.23D

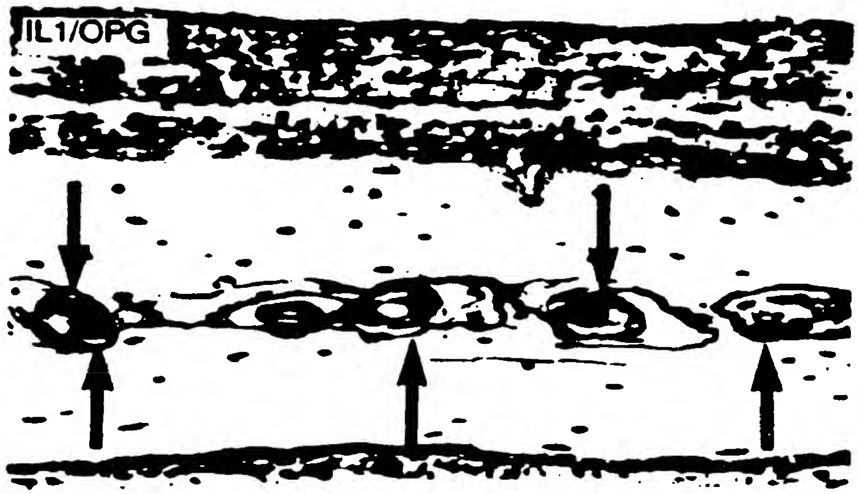
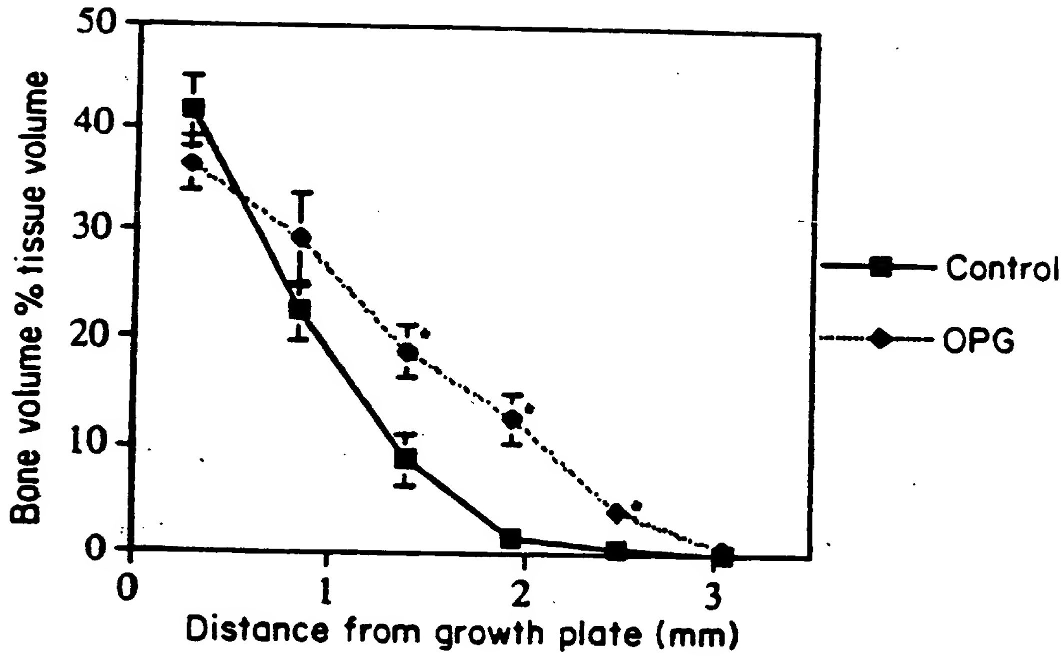


FIG.24A

FIG.24B

FIG.25



* Different to control $p < 0.01$

FIG.26A

FIG.26.B

FIG.27

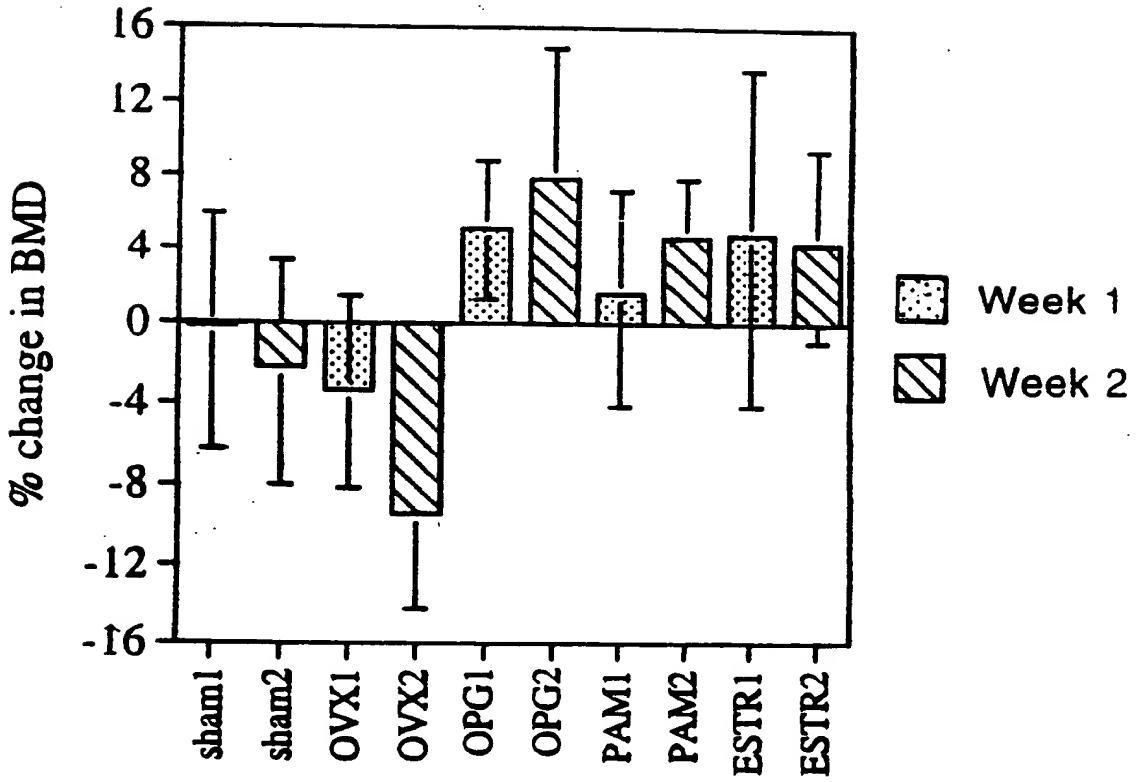
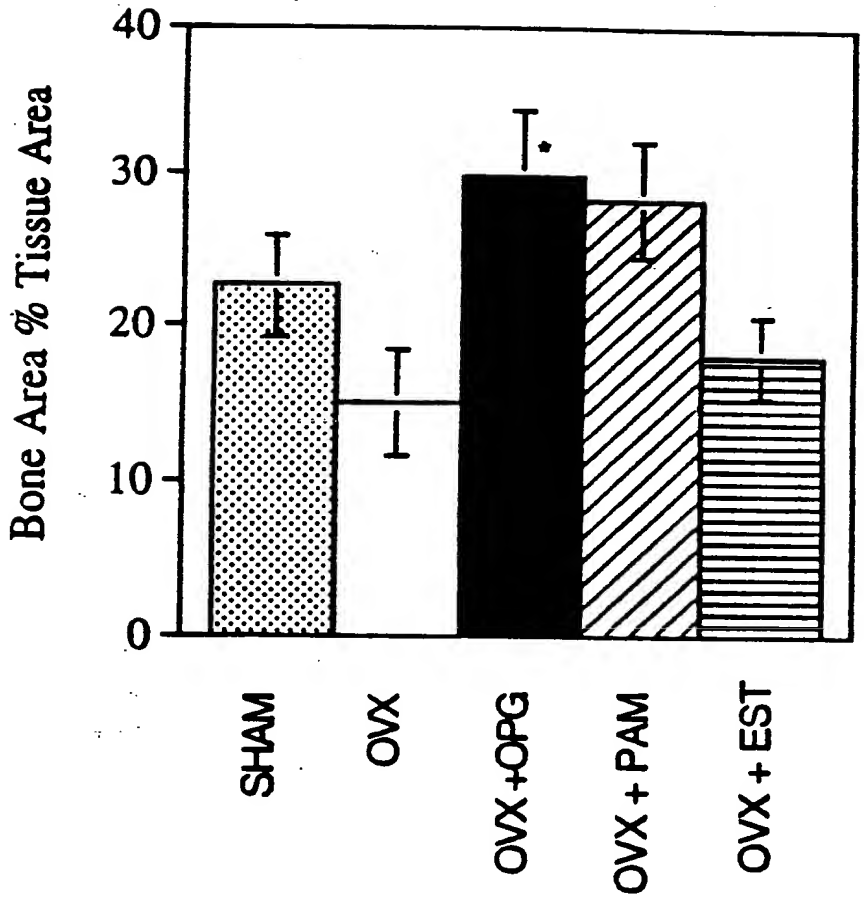

16
12
8
4
0
-4
-8
-12
-16
% change in BMD
sham1
sham2
OVX1
OVX2
OPG1
OPG2
PAM1
PAM2
ESTR1
ESTR2
Week 1
Week 2

FIG.28



* Different to OVX $p < 0.05$

Figure 29A

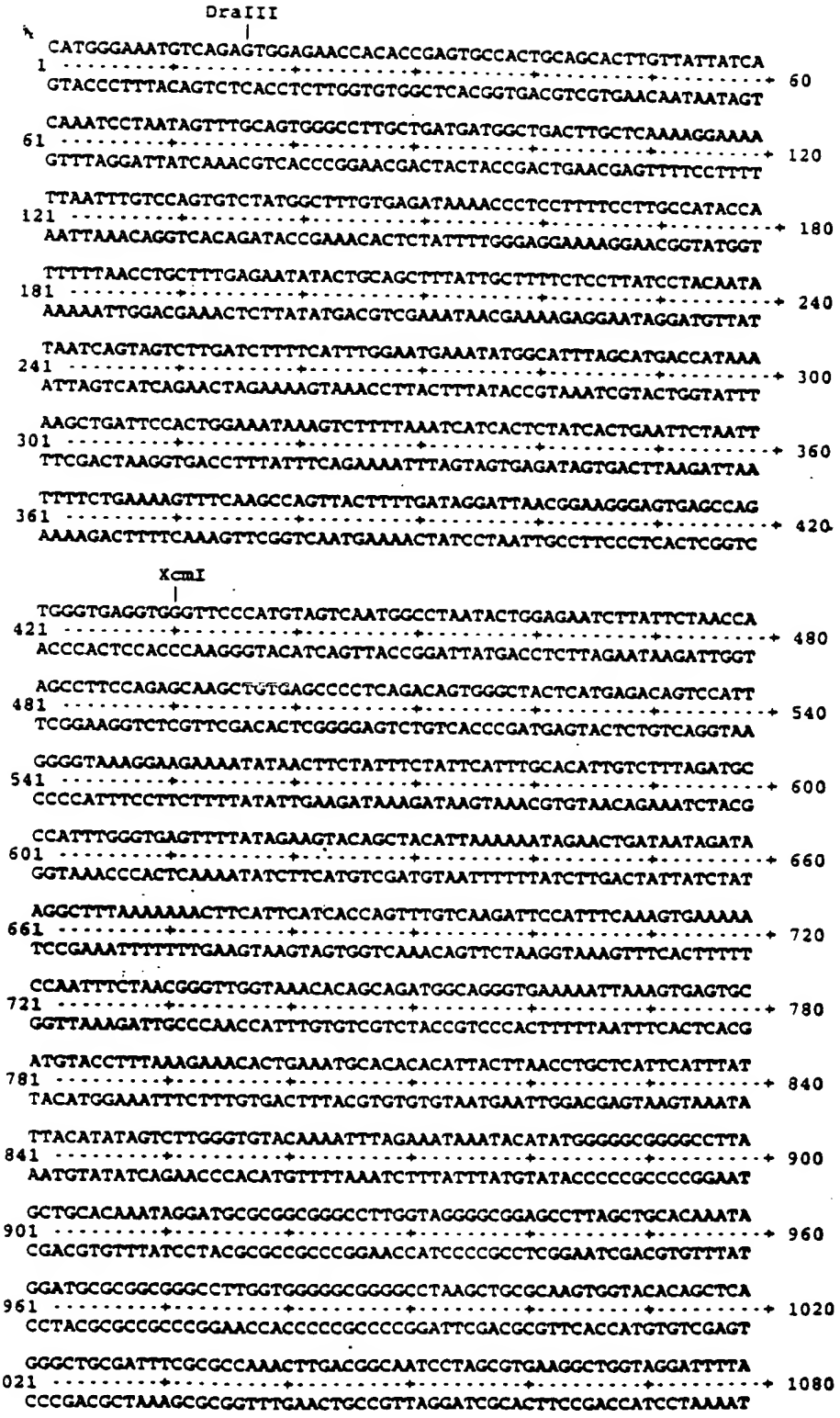


Figure 29B

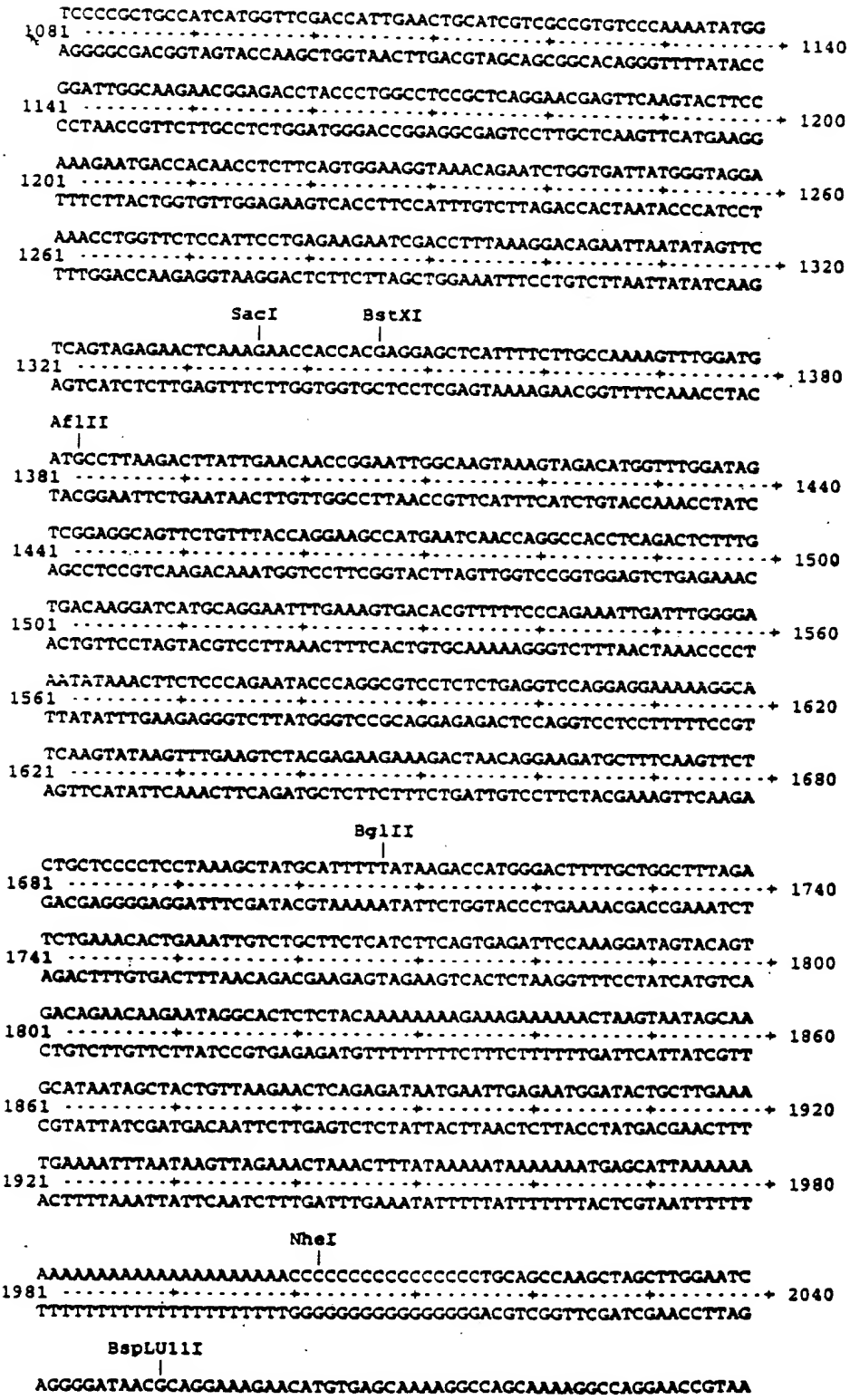

TCCCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGG
1081
AGGGGCGACGGTAGTACCAAGCTGGTAACTTGACGTAGCAGCGGCACAGGGTTTTATACC
1140
GGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCC
1141
CCTAACCGTTCTTGCCTCTGGATGGGACCGGAGGCGAGTCCTTGCTCAAGTTCATGAAGG
1200
AAAGAATGACCACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGA
1201
TTTCTTACTGGTGTTGGAGAAGTCACCTTCCATTTGTCTTAGACCACTAATACCCATCCT
1260
AAACCTGGTTCTCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTTC
1261
TTTGGACCAAGAGGTAAGGACTCTTCTTAGCTGGAAATTTCCTGTCTTAATTATATCAAG
1320
SacI
BstXI
TCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGGATG
1321
AGTCATCTCTTGAGTTTCTTGGTGGTGCTCCTCGAGTAAAAGAACGGTTTTCAAACCTAC
1380
AflII
ATGCCTTAAGACTTATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAG
1381
TACGGAATTCTGAATAACTTGTTGGCCTTAACCGTTCATTTCATCTGTACCAAACCTATC
1440
TCGGAGGCAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTG
1441
AGCCTCCGTCAAGACAAATGGTCCTTCGGTACTTAGTTGGTCCGGTGGAGTCTGAGAAAC
1500
TGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTGGGGA
1501
ACTGTTCCTAGTACGTCCTTAAACTTTCACTGTGCAAAAAGGGTCTTTAACTAAACCCCT
1560
AATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCA
1561
TTATATTTGAAGAGGGTCTTATGGGTCCGCAGGAGAGACTCCAGGTCCTCCTTTTTCCGT
1620
TCAAGTATAAGTTTGAAGTCTACGAGAAGAAAGACTAACAGGAAGATGCTTTCAAGTTCT
1621
AGTTCATATTCAAACTTCAGATGCTCTTCTTTCTGATTGTCCTTCTACGAAAGTTCAAGA
1680
BglII
CTGCTCCCCTCCTAAAGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGCTTTAGA
1681
GACGAGGGGGAGGATTTCGATACGTAAAAATATTCTGGTACCCTGAAAACGACCGAAATCT
1740
TCTGAAACACTGAAATTGTCTGCTTCTCATCTTCAGTGAGATTCCAAAGGATAGTACAGT
1741
AGACTTTGTGACTTTAACAGACGAAGAGTAGAAGTCACTCTAAGGTTTCCTATCATGTCA
1800
GACAGAACAAGAATAGGCACTCTCTACAAAAAAAAAGAAAGAAAAAACTAAGTAATAGCAA
1801
CTGTCTTGTTCTTATCCGTGAGAGATGTTTTTTTTCTTTCTTTTTTGATTCATTATCGTT
1860
GCATAATAGCTACTGTTAAGAACTCAGAGATAATGAATTGAGAATGGATACTGCTTGAAA
1861
CGTATTATCGATGACAATTCTTGAGTCTCTATTACTTAACTCTTACCTATGACGAACTTT
1920
TGAAAATTTAATAAGTTAGAAACTAAACTTTATAAAAATAAAAAAATGAGCATTAAAAAA
1921
ACTTTTAAATTATTCAATCTTTGATTTGAAATATTTTTATTTTTTTACTCGTAATTTTTT
1980
NheI
AAAAAAAAAAAAAAAAAAAAAACCCCCCCCCCCCCCCCCTGCAGCCAAGCTAGCTTGGAATC
1981
TTTTTTTTTTTTTTTTTTTTTGGGGGGGGGGGGGGGGGACGTCGGTTCGATCGAACCTTAG
2040
BspLU11I
AGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAA

Figure 29C

```
2041 ---------+---------+---------+---------+---------+---------+ 2100
     TCCCCTATTGCGTCCTTTCTTGTACACTCGTTTTCCGGTCGTTTTCCGGTCCTTGGCATT

     AAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAA
2101 ---------+---------+---------+---------+---------+---------+ 2160
     TTTCCGGCGCAACGACCGCAAAAAGGTATCCGAGGCGGGGGGACTGCTCGTAGTGTTTTT

     TCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC
2161 ---------+---------+---------+---------+---------+---------+ 2220
     AGCTGCGAGTTCAGTCTCCACCGCTTTGGGCTGTCCTGATATTTCTATGGTCCGCAAAGG

     CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTC
2221 ---------+---------+---------+---------+---------+---------+ 2280
     GGGACCTTCGAGGGAGCACGCGAGAGGACAAGGCTGGGACGGCGAATGGCCTATGGACAG

     CGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAG
2281 ---------+---------+---------+---------+---------+---------+ 2340
     GCGGAAAGAGGGAAGCCCTTCGCACCGCGAAAGAGTATCGAGTGCGACATCCATAGAGTC

     TTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGA
2341 ---------+---------+---------+---------+---------+---------+ 2400
     AAGCCACATCCAGCAAGCGAGGTTCGACCCGACACACGTGCTTGGGGGGCAAGTCGGGCT

     CCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC
2401 ---------+---------+---------+---------+---------+---------+ 2460
     GGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGGCCATTCTGTGCTGAATAG

     GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTAC
2461 ---------+---------+---------+---------+---------+---------+ 2520
     CGGTGACCGTCGTCGGTGACCATTGTCCTAATCGTCTCGCTCCATACATCCGCCACGATG

     AGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTG
2521 ---------+---------+---------+---------+---------+---------+ 2580
     TCTCAAGAACTTCACCACCGGATTGATGCCGATGTGATCTTCCTGTCATAAACCATAGAC

     CGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACA
2581 ---------+---------+---------+---------+---------+---------+ 2640
     GCGAGACGACTTCGGTCAATGGAAGCCTTTTTCTCAACCATCGAGAACTAGGCCGTTTGT

     HgiEII
       |
     AACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAA
2641 ---------+---------+---------+---------+---------+---------+ 2700
     TTGGTGGCGACCATCGCCACCAAAAAAACAAACGTTCGTCGTCTAATGCGCGTCTTTTTT

     AGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA
2701 ---------+---------+---------+---------+---------+---------+ 2760
     TCCTAGAGTTCTTCTAGGAAACTAGAAAAGATGCCCCAGACTGCGAGTCACCTTGCTTTT

     CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTT
2761 ---------+---------+---------+---------+---------+---------+ 2820
     GAGTGCAATTCCCTAAAACCAGTACTCTAATAGTTTTTCCTAGAAGTGGATCTAGGAAAA

     AAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAG
2821 ---------+---------+---------+---------+---------+---------+ 2880
     TTTAATTTTTACTTCAAAATTTAGTTAGATTTCATATATACTCATTTGAACCAGACTGTC

     TTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT
2881 ---------+---------+---------+---------+---------+---------+ 2940
     AATGGTTACGAATTAGTCACTCCGTGGATAGAGTCGCTAGACAGATAAAGCAAGTAGGTA

     AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCC
2941 ---------+---------+---------+---------+---------+---------+ 3000
     TCAACGGACTGAGGGGCAGCACATCTATTGATGCTATGCCCTCCCGAATGGTAGACCGGG

     CAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAA
3001 ---------+---------+---------+---------+---------+---------+ 3060
     GTCACGACGTTACTATGGCGCTCTGGGTGCGAGTGGCCGAGGTCTAAATAGTCGTTATTT

     CCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCA
3061 ---------+---------+---------+---------+---------+---------+ 3120
     GGTCGGTCGGCCTTCCCGGCTCGCGTCTTCACCAGGACGTTGAAATAGGCGGAGGTAGGT

     GTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAA
3121 ---------+---------+---------+---------+---------+---------+ 3180
     CAGATAATTAACAACGGCCCTTCGATCTCATTCATCAAGCGGTCAATTATCAAACGCGTT
```

Figure 29D

```
     CGTTGTTGCCATTGCTGCAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATT
3181 ---------+---------+---------+---------+---------+---------+ 3240
     GCAACAACGGTAACGACGTCCGTAGCACCACAGTGCGAGCAGCAAACCATACCGAAGTAA

     CAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGC
3241 ---------+---------+---------+---------+---------+---------+ 3300
     GTCGAGGCCAAGGGTTGCTAGTTCCGCTCAATGTACTAGGGGGTACAACACGTTTTTTCG

                          EaeI
                PvuI      GdiII
                |         |
     GGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACT
3301 ---------+---------+---------+---------+---------+---------+ 3360
     CCAATCGAGGAAGCCAGGAGGCTAGCAACAGTCTTCATTCAACCGGCGTCACAATAGTGA

     CATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTC
3361 ---------+---------+---------+---------+---------+---------+ 3420
     GTACCAATACCGTCGTGACGTATTAAGAGAATGACAGTACGGTAGGCATTCTACGAAAAG

                      BcgI
                      |
     TGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTG
3421 ---------+---------+---------+---------+---------+---------+ 3480
     ACACTGACCACTCATGAGTTGGTTCAGTAAGACTCTTATCACATACGCCGCTGGCTCAAC

     CTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCT
3481 ---------+---------+---------+---------+---------+---------+ 3540
     GAGAACGGGCCGCAGTTGTGCCCTATTATGGCGCGGTGTATCGTCTTGAAATTTTCACGA

     CATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATC
3541 ---------+---------+---------+---------+---------+---------+ 3600
     GTAGTAACCTTTTGCAAGAAGCCCCGCTTTTGAGAGTTCCTAGAATGGCGACAACTCTAG

     CAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAG
3601 ---------+---------+---------+---------+---------+---------+ 3660
     GTCAAGCTACATTGGGTGAGCACGTGGGTTGACTAGAAGTCGTAGAAAATGAAAGTGGTC

     CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGAC
3661 ---------+---------+---------+---------+---------+---------+ 3720
     GCAAAGACCCACTCGTTTTTGTCCTTCCGTTTTACGGCGTTTTTTCCCTTATTCCCGCTG

                      SspI
                      |
     ACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGG
3721 ---------+---------+---------+---------+---------+---------+ 3780
     TGCCTTTACAACTTATGAGTATGAGAAGGAAAAAGTTATAATAACTTCGTAAATAGTCCC

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3781 ---------+---------+---------+---------+---------+---------+ 3840
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     TCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGAC
3841 ---------+---------+---------+---------+---------+---------+ 3900
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     ATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTTCGTCTTCAAGAATTCCCTGTGGA
3901 ---------+---------+---------+---------+---------+---------+ 3960
     TAATTGGATATTTTTATCCGCATAGTGCTCCGGGAAAGCAGAAGTTCTTAAGGGACACCT

     ATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAA
3961 ---------+---------+---------+---------+---------+---------+ 4020
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     GCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCA
4021 ---------+---------+---------+---------+---------+---------+ 4080
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     GAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGC
4081 ---------+---------+---------+---------+---------+---------+ 4140
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     CCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTT
4141 ---------+---------+---------+---------+---------+---------+ 4200
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```

Figure 29E

```
                      SfiI
                      |
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            AvrII
            |
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     CACGCGCCCGCCGCCCTACCTGAGGCCGCCATCCACGCCGGTTGAGTCGCGTTCTGCCGC
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     CTCCCGCCTGTGGTGCCTCCTGAACTGCGTCCGCCGTCTAGGTAAGTTTAAAGCTCAGGT
4381 ---------+---------+---------+---------+---------+---------+ 4440
     GAGGGCGGACACCACGGAGGACTTGACGCAGGCGGCAGATCCATTCAAATTTCGAGTCCA

                                    NgoAIV
                                    |
     CGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCCTACCTAGACTCAGCCGGCTCTCCA
4441 ---------+---------+---------+---------+---------+---------+ 4500
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     CGCTTTGCCTGACCCTGCTTGCTCAACTCTACGTCTTTGTTTCGTTTTCTGTTCTGCGCC
4501 ---------+---------+---------+---------+---------+---------+ 4560
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                        HpaI
                        |
     GTTACAGATCCGTCGAGGAACTGAAAAACCAGAAAGTTAACTGGTAAGTTTAGTCTTTTT
4561 ---------+---------+---------+---------+---------+---------+ 4620
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        PspSII BamHI
          |      |
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  HindIII XbaI           BssHII
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b     S  I  K  W  T  T  Q  E  T  F  P  P  K  Y  L  H  Y  D  E  E  -

                              KpnI
                              |
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09/871,960

Figure 29F

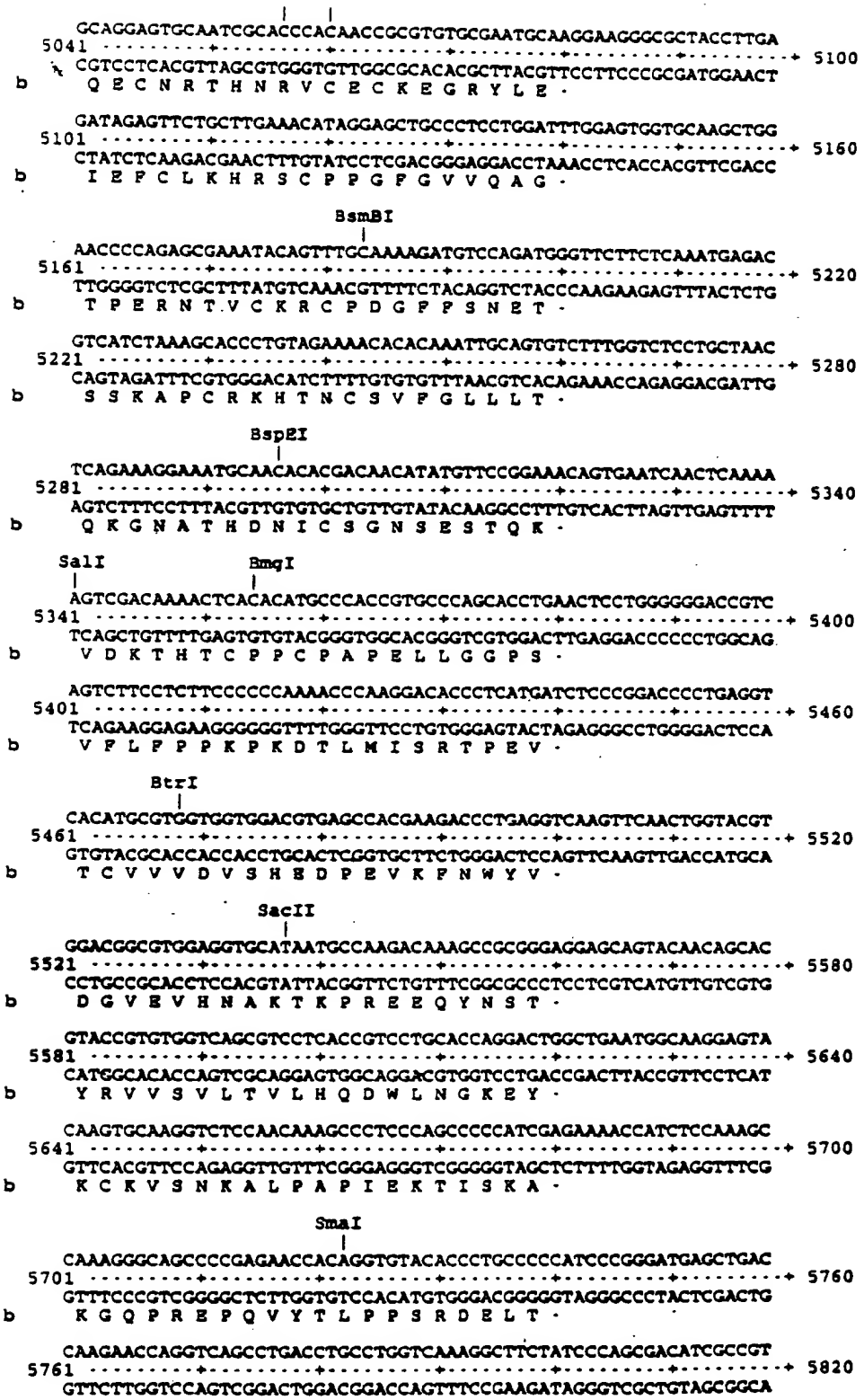
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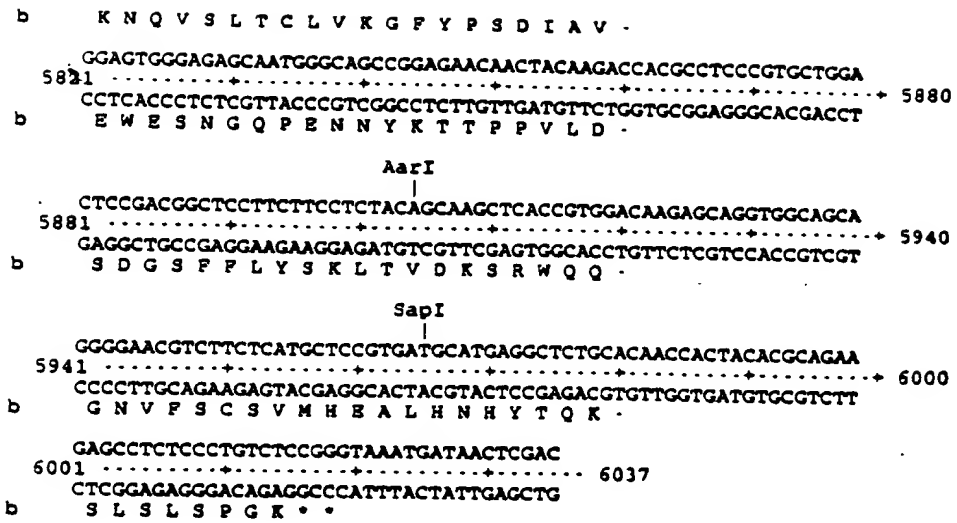
Figure 29G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6001
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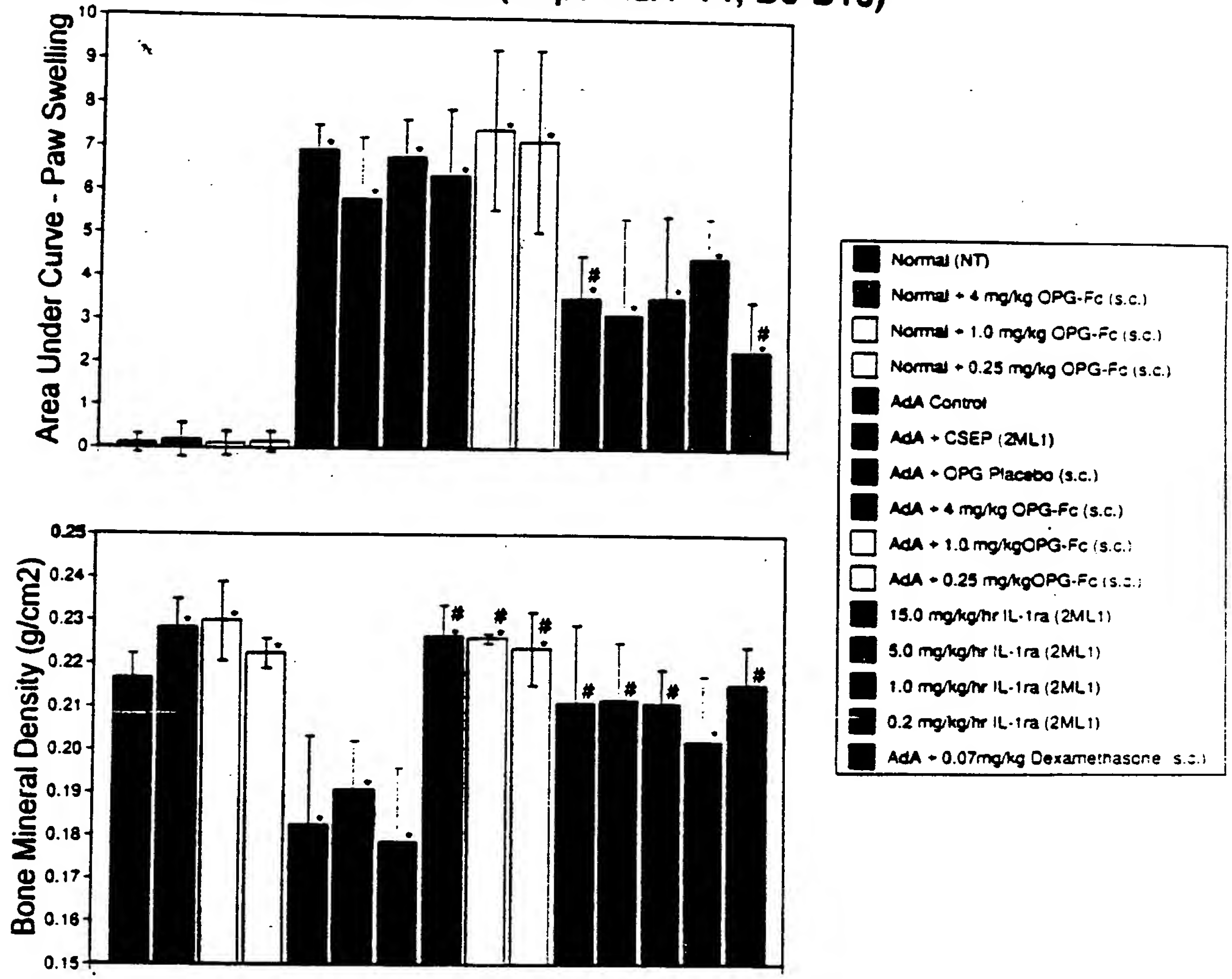
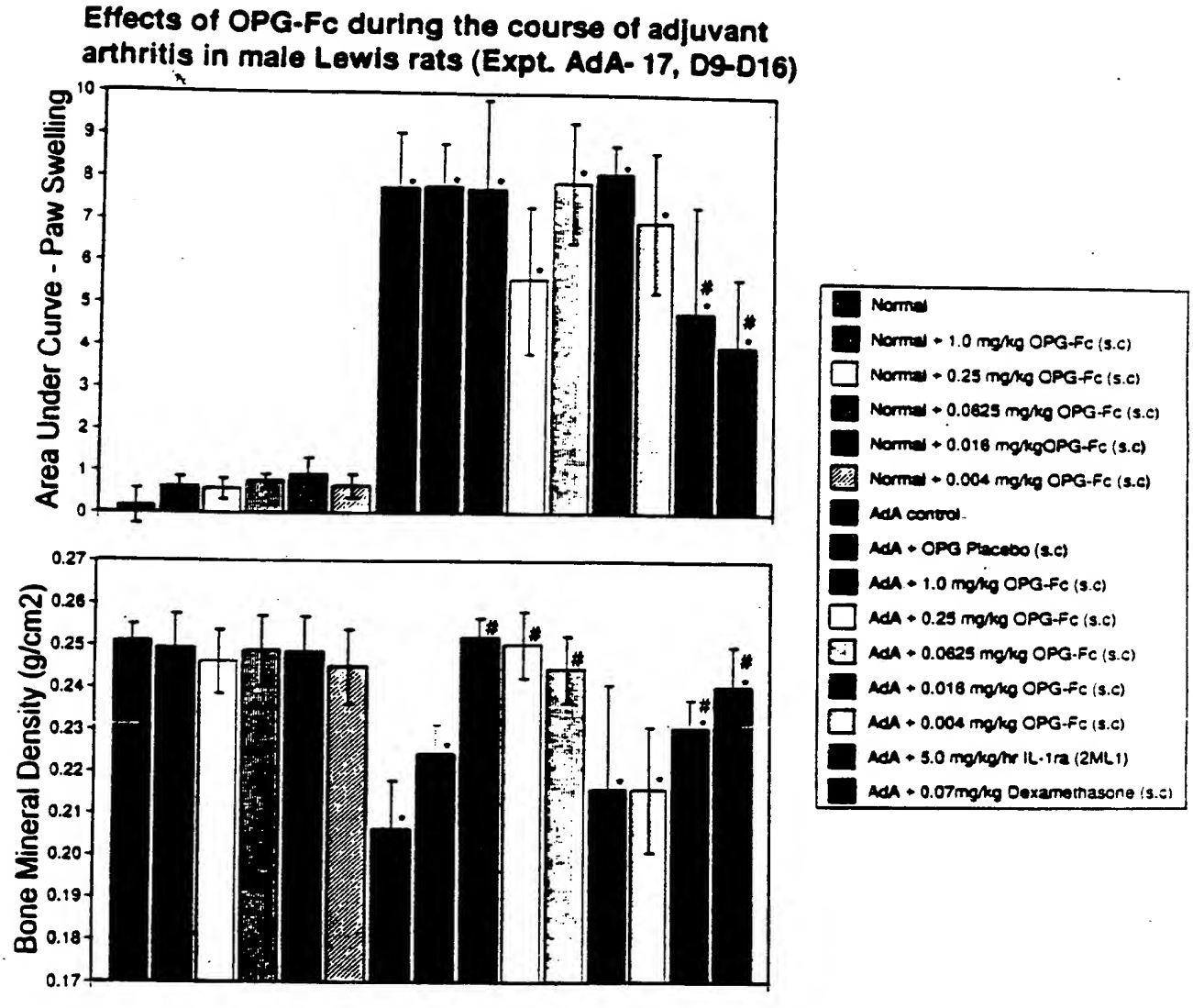
Figure 30A

Effects of OPG-Fc during the course of adjuvant arthritis in male Lewis rats (Expt. AdA- 14, D9-D16)



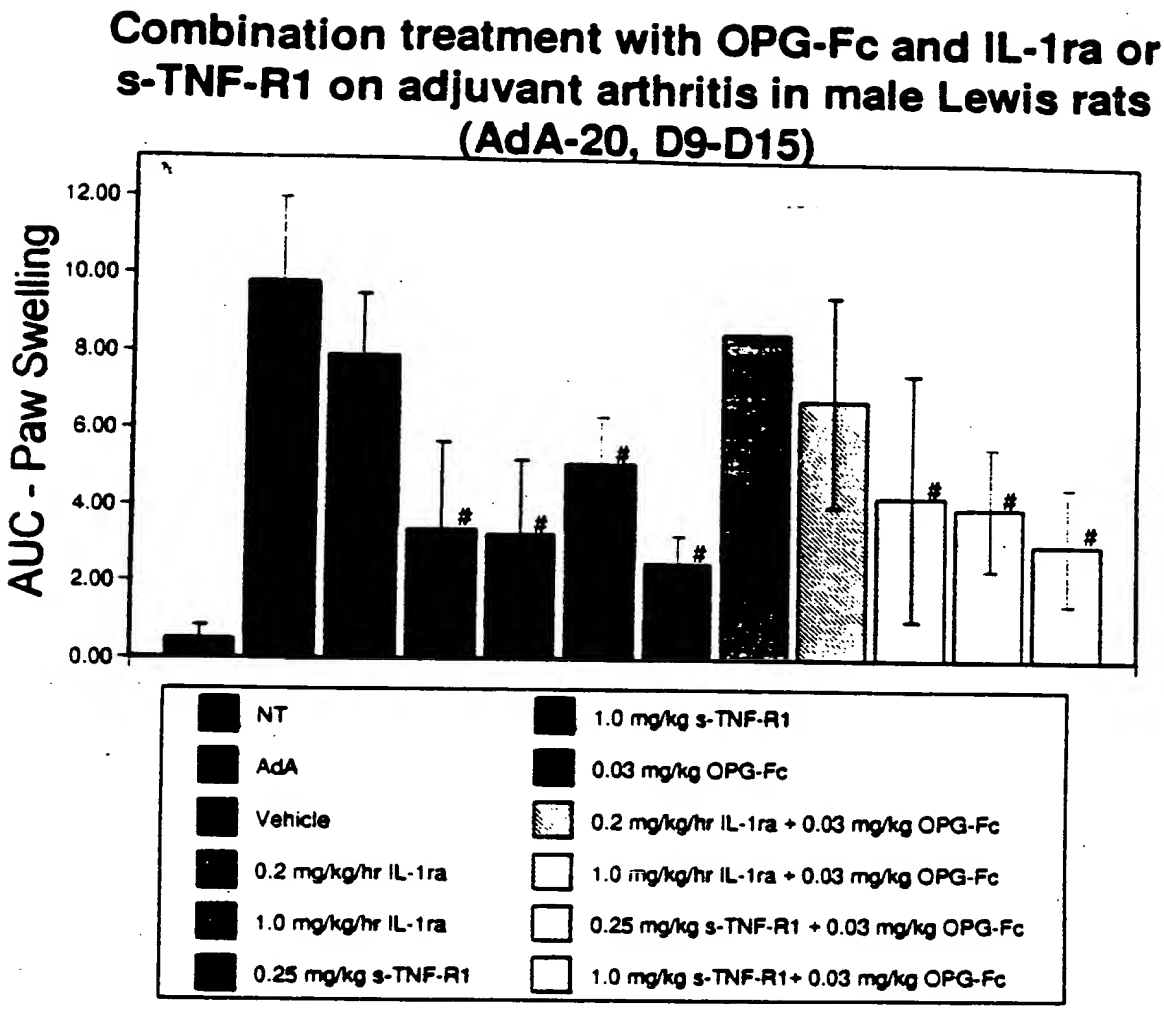
Paws from rats with adjuvant arthritis induced by 0.5mg mycobacteria in oil were analyzed by DEXA for BMD. Evaluation of BMD, a 29mm X 25mm box was centered at the calcaneus (expt AdA-14 2/99, Amgen nb#22957 p47-49).
* compared to normal, # compared to vehicle*
P < 0.05 Mann-Whitney U test

Figure 30B



Paws from rats with adjuvant arthritis induced by 0.5mg mycobacteria in oil were analyzed by DEXA for BMD. Evaluation of BMD, a 29mm X 25mm box was centered at the calcaneus (expt AdA -17 3/99, Amgen nb#22957 p62-65).
* compared to normal, # compared to vehicle
$P < 0.05$ Mann-Whitney U test

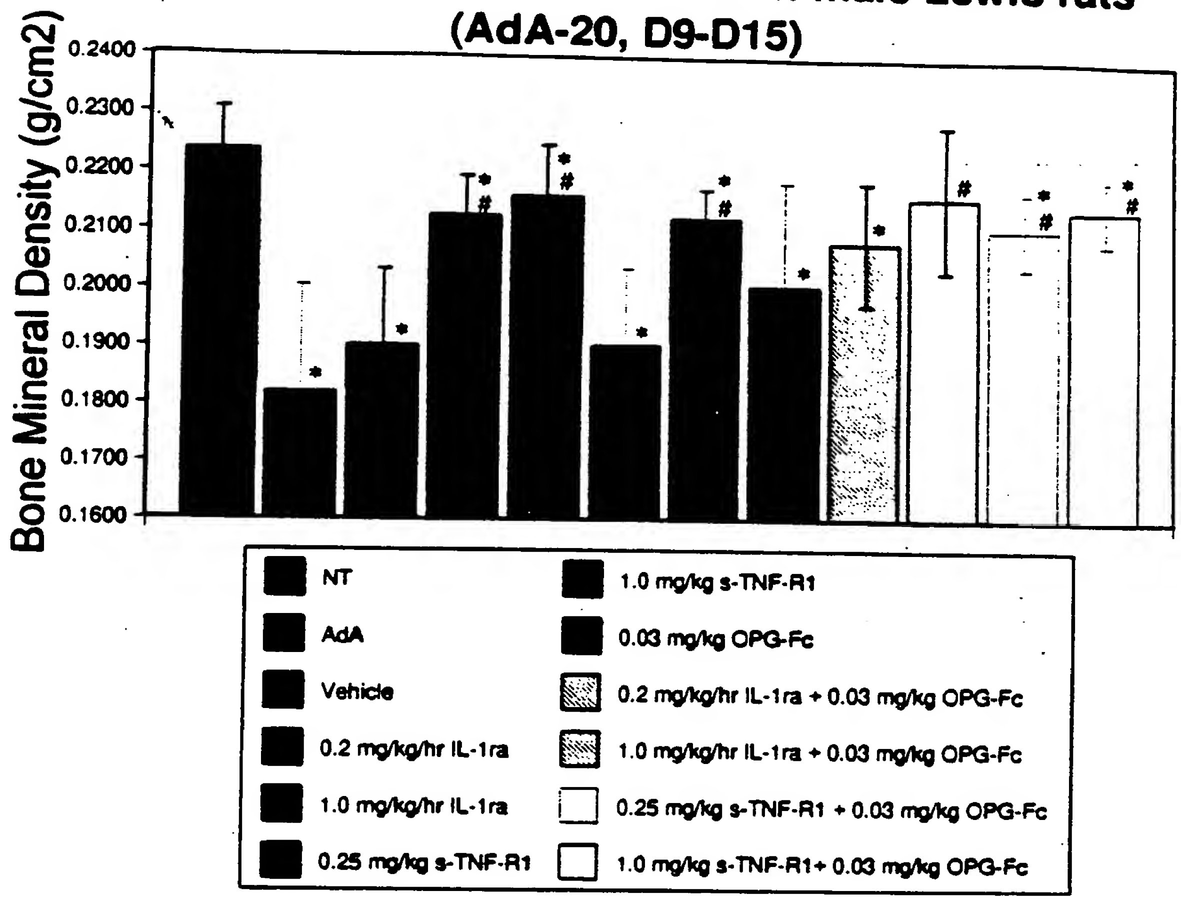
Figure 31A



Paws from rats with adjuvant arthritis induced by 0.5mg mycobacteria in oil were analyzed by DEXA for BMD. (expt AdA-20 5/99, Amgen nb#22957 p84).
* compared to normal, # compared to vehicle
$P < 0.05$ Mann-Whitney U test.
All groups are significant vs normal

Figure 31B

Combination treatment with OPG-Fc and IL-1ra or s-TNF-R1 on adjuvant arthritis in male Lewis rats (AdA-20, D9-D15)



Paws from rats with adjuvant arthritis induced by 0.5mg mycobacteria in oil were analyzed by DEXA for BMD. Evaluation of BMD, a 29mm X 25mm was centered at the tibiotarsal region. (expt AdA-20 5/99, Amgen nb#22957 p88).

* compared to normal, # compared to vehicle

.P < 0.05 Mann-Whitney U test